ARCHIVES OF

NEUROLOGY AND PSYCHIATRY

EDITORIAL BOARD

T. H. WEISENBURG, Philadelphia
SAMUEL T. ORTON, Iowa City
H. DOUGLAS SINGER, Chicago
STANLEY COBB, Boston
E. W. TAYLOR, Boston
FREDERICK TILNEY, New York

VOLUME 15
1926

PUBLISHERS
AMERICAN MEDICAL ASSOCIATION
CHICAGO, ILL.

Hosp. Lib. (Ben-Cerr)
gt - various sources

CONTENTS OF VOLUME 15

JANUARY, 1926. NUMBER 1

PAGE

Neuron Destruction in Postencephalitic Paralysis Agitans: A Micrometric Study of the Lenticular Region and Substantia Nigra. J. Charnley McKinley, M.D., Minneapolis, and Lawrence R. Gowan, M.D., Duluth 1

Cerebral Symptoms Induced by Angioneurotic Edema. Foster Kennedy, M.D., F.R.S.E., New York 28

Trichinosis Encephalitis: A Pathologic Study. George B. Hassin, M.D., and Isadore B. Diamond, M.D., Chicago 34

Differential Diagnosis Between Cerebral Degeneration, Infiltrating Cerebral Neoplasm and Infiltrating Cerebral Neoplasm with Degeneration. Henry Alsop Riley, M.D., and Charles A. Elsberg, M.D., New York .. 48

Brain Repair. Richard B. Wilson, M.D., Boston 75

Hypophysial Fat Dystrophy with Hyperglycemia and Glycosuria: Report of a Case. Shepard Shapiro, M.D., and Mark G. Kliatshco, M.D., New York 85

Roentgen-Ray Treatment of Pituitary Tumors. E. B. Towne, M.D., San Francisco 92

The Amyostatic Syndrome of Epidemic Encephalitis: Blood Sugar Tolerance Studies. Theophile Raphael, M.D., Olive M. Searle, M.S., and William G. Ferguson, M.D., Ann Arbor, Mich 103

Clinical and Occasional Notes:

Thrombosis of the Rolandic Vein: Report of Case. Charles Edward Dowman, M.D., Atlanta, Georgia 110

News and Comments:

Congress of Alienists and Neurologists of France and of French Speaking Countries 113

Abstracts from Current Literature 114

Society Transactions:

New York Neurological Society 135

Book Reviews 148

FEBRUARY, 1926. NUMBER 2

The Oedipus Complex: An Attempt to Estimate Its Rôle and Importance. William McDougall, M.B., Cambridge, Mass 151

Behavior Origins from a Physiologic Point of View. C. M. Child, Chicago 173

Behaviorism: A Psychology Based on Reflexes. John B. Watson, Ph.D., M.D., New York 185

Sarcomatosis of the Brain. B. M. Fried, M.D., Boston 205

Parkinsonian States: Clinico-Pathologic Studies. G. B. Hassin, M.D., and Peter Bassoe, M.D., Chicago 218

Psychoses Occurring During the Puerperium. Edward A. Strecker, M.D., Philadelphia, and Franklin G. Ebaugh, M.D., Denver 239

The Psychiatric Value of the Kuhlmann Tests. James S. Plant, S.M., M.D., Newark, N. J 253

Obituary:

John Henry Wallace Rhein, M.D., Ph.G 260

Abstracts from Current Literature 262

Book Reviews 278

MARCH, 1926. NUMBER 3

PAGE

The Meninges in Lower Vertebrates Compared with Those in Mammals. C. U. Ariëns Kappers, M.D., Amsterdam, Netherlands 281

Encephalitis Periaxialis Diffusa of Schilder: Report of a Case. Samuel Brock, M.D.; Patrick M. Carroll, M.D., and Lewis Stevenson, M.D., New York 297

The Spontaneous Escape of Cerebrospinal Fluid Through the Nose: Its Occurrence with Brain Tumor. C. E. Locke, Jr., M.D., Cleveland 309

Bulbocapnin: Its Use in the Treatment of Tremor and in the Experimental Production of Basal Ganglion Symptomatology. Hugo Mella, M.D., Boston 325

The Presence of an Oxytocic Substance (Posterior Hypophysis Extract) in Cerebrospinal Fluid. Shepard Shapiro, M.D., New York 331

Toxemias Occurring in the Early Stages of Mental Disease. Howard D. McIntyre, M.D., Aurelia P. McIntyre, M.D., and Robert J. Norris, Cincinnati 341

The Spinal Fluid in Epilepsy: A Study of Fifty Cases. Harold A. Patterson, M.D., and Paul Levi, M.D., Sonyea, N. Y. 353

Xanthochromia in Epidemic Encephalitis: Report of Three Cases. David Rothschild, M.D., Boston 365

Difficult Urination Associated with Intracranial Tumors of the Posterior Fossa: A Physiologic and Clinical Study. Emile Holman, M.D., Cleveland 371

News and Comment:
Fifty-Second Annual Meeting of the American Neurological Association 381
The National Association for the Study of Epilepsy 381
The American Psychiatric Association 381

Abstracts from Current Literature 382

Society Transactions:
Philadelphia Neurological Society 400

Book Reviews 405

APRIL, 1926. NUMBER 4

A Contribution to the Pathology of Paralysis Agitans. Charles Metcalfe Byrnes, M.D., Baltimore 407

Sensory Disturbances in Tumors of the Cervical Spinal Cord: Arrangement of the Fibers in the Sensory Pathways. Frederick Tilney, M.D., and Charles A. Elsberg, M.D., New York 444

Gross Pontile Bleeding in Traumatic and Nontraumatic Cerebral Lesions. George Wilson, M.D., and N. W. Winkelman, M.D., Philadelphia 455

The Correction of Colloidal Gold Solutions as Applied to the Lange Reaction: A Simple and Accurate Titration Method. N. Novick, Bronx, N. Y. 471

Clinical and Occasional Notes:
Delayed Post-Traumatic Intracranial Compression. Abraham O. Wilensky, M.D., New York 475

Obituary:
Henry Rust Stedman, M.D 480

News and Comment:
Fifty-Second Annual Meeting of the American Neurological Association 483
The National Association for the Study of Epilepsy 483
The American Psychiatric Association 483

Abstracts from Current Literature 484

Society Transactions:
New York Neurological Society with the Section of Neurology and Psychiatry of the Academy of Medicine 515
The Chicago Neurological Society 523
Philadelphia Neurological Society 527

Book Reviews 533

MAY, 1926. NUMBER 5

PAGE

Sensory Disturbances in Multiple Sclerosis: Their Significance in Diagnosis. Otto Sittig, M.D., Prague, Czechoslovakia 537

The Development of the Meninges. Samuel C. Harvey, M.D., and Harold S. Burr, Ph.D., New Haven, Conn 545

Vascular Lesions and Tumors of the Brain; Difficulties in Differential Diagnosis. Report of Seven Cases with Necropsy Findings. Joseph H. Globus, M.D., and Israel Strauss, M.D., New York 568

Studies of Casts of the Cerebral Ventricles. C. E. Locke, Jr., M.D., Cleveland 588

The Constant Relation Between Postures of Motile and Rigid States. Walter M. Kraus, M.D., New York 597

The Radix Spinalis Trigemini and the Principle of Usurpation. Walter Freeman, M.D., Washington, D. C 607

Neurologic Symptoms in Osteitis Deformans (Paget's Disease). Donald Gregg, M.D., Wellesley, Mass 613

Clinical and Occasional Notes:

Respiratory Disturbances Following Epidemic Encephalitis. William A. Smith, M.D., Ann Arbor, Mich 617

Obituary:

Prof. Camillo Golgi 623

News and Comment:

Fifty-Second Annual Meeting of the American Neurological Association 628

The National Association for the Study of Epilepsy 628

The American Psychiatric Association 628

Abstracts from Current Literature 629

Society Transactions:

Boston Society of Psychiatry and Neurology 652

New York Neurological Society and the Section of Neurology and Psychiatry of the Academy of Medicine 661

Chicago Neurological Society 667

Philadelphia Neurological Society 672

Book Reviews 674

JUNE, 1926. NUMBER 6

The Story of the Glossopharyngeal Nerve, and Four Centuries of Research Concerning the Cranial Nerves of Man. Charles L. Dana, M.D., New York 675

Human Adult and Embryo Anterior Horn Cells: A Comparison of Form in Relation to the Concept of Neurobiotaxis. Walter M. Kraus, M.D., and Arthur Weil, M.D., New York 686

A Case of Cervicodorsal Spina Bifida Occulta, with Trophic and Sensory Disturbances and Cervical Hypertrichosis. Mario Gozzano, M.D., Rome, Italy 702

Further Studies on the Etiology of Epidemic Hiccup (Singultus) and Its Relation to Encephalitis. Edward C. Rosenow, M.D., Rochester, Minn. 712

A Case of Hydrophobia with Negri Bodies in the Brain. Henry R. Viets, M.D., Boston 735

Significant Chemical Changes in the Spinal Fluid in Meningitis, with Special Reference to Lactic Acid Content. Michael Osnato, M.D., and John A. Killian, Ph. D., New York 738

Yellow Spinal Fluid Associated with Tumor of the Brain. Mandred W. Comfort, M.D., Rochester, Minn 751

Clinical and Occasional Notes:

Fixation of the Cells of the Cerebrospinal Fluid with Iodine Vapor. Robert S. Cunningham, M.D., and Lawrence S. Kubie, M.D., Baltimore 761

PAGE

Special Article:
Neuropathology: Lecture Notes. Samuel T. Orton, A.M., M.D., Iowa City 763

Editorial:
Association for Research in Nervous and Mental Disease..... 776

News and Comment..... 778

Abstracts from Current Literature..... 779

Society Transactions:
Boston Society of Psychiatry and Neurology..... 795
New York Neurological Society..... 802
Société de Neurologie de Paris..... 817

Book Review 825

General Index 827

Hospital Library
Hosp. Lib

VOLUME 15 NUMBER 1

ARCHIVES OF NEUROLOGY AND PSYCHIATRY

EDITORIAL BOARD

T. H. WEISENBURG, Philadelphia
SAMUEL T. ORTON, Iowa City — H. DOUGLAS SINGER, Chicago
HUGH T. PATRICK, Chicago — R. W. TAYLOR, Boston
FREDERICK TILNEY, New York

JANUARY, 1926

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, Jan. 7, 1919, at the Postoffice at Chicago, Illinois, Under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of Oct. 3, 1917, authorized Jan. 15, 1919.

CONTENTS OF PREVIOUS NUMBERS

NOVEMBER, 1925. NUMBER 5

"Word-Blindness" in School Children. Samuel T. Orton, A.M., M.D., Iowa City.

Closed Foramina of Luschka in the Brains of the Insane: Their Influence on the Pathogenesis of the Psychoses. J. Fremont Bateman, M.A., Cincinnati.

Is Encephalitis an Infectious, Epidemic Disease? S. R. Salzman, M.D., Toledo, Ohio.

Reactive Gliosis in a Case of Brain Tumor. Walter Freeman, M.D., Washington, D. C.

Psychosis Associated with Trauma of the Head: Report of a Case of Trauma Sustained in Infancy and Determining a Later Developing Dural Tumor. A. E. Taft, M.D., and E. A. Strecker, M.D., Philadelphia.

Significance of "Accessory" Behavior Accompanying Vocal Reactions. Leslie B. Hohman, A.B., M.D., Baltimore.

Motor Disturbances in Peripheral Nerve Lesions: (A) Muscles Involved in Partial Lesions; (B) Order of Restored Motion. Lewis J. Pollock, M.D., Chicago.

News and Comment:
Program for Meeting of Association for Research in Nervous and Mental Disease.

Abstracts from Current Literature.

Society Transactions:
Chicago Neurological Society.
Société de Neurologie de Paris.
New York Neurological Society.

Book Reviews.

DECEMBER, 1925. NUMBER 6

General Significance of Tay-Sachs Disease. Prof. Charles Schaffer, Budapest, Hungary.

Breech Delivery in Its Possible Relations to Injury of the Spinal Cord, with Special Reference to Infantile Paraplegia. F. R. Ford, M.D., Baltimore.

New Method of Recording Muscular Tremors. Charles G. Beall, M.D., Fort Wayne, Ind.

Clinical Application of Tonic Neck Reflexes, with Special Reference to Tuberculous Meningitis. I. S. Wechsler, M.D., and S. Brock, M.D., New York.

Behavior Disorders in Children: Psychologic Examination. Bert I. Beverly, M.D., Chicago.

Behavior Disorders in Children: Medical Aspects. Herman M. Adler, M.D., Chicago.

Behavior Disorders in Children: Psychanalytic Studies. David M. Levy, M.D., Chicago.

A Study of the Vibratory Sensation. Richard S. Ahrens, B.S., M.D., Minneapolis.

Lumbar Puncture Headache. Bernard J. Alpers, M.D., Philadelphia.

Spina Bifida Occulta Cervicalis: Report of a Case. George B. Hassin, M.D., Chicago.

Basal Metabolism in Mental Disease. K. M. Bowman, M.D., and C. C. Fry, M.D., Boston.

Clinical and Occasional Notes:
Congenital Total Hemihypertrophy. Elias A. Reed, M.D., New York.

Abstracts from Current Literature.

Book Reviews.

Index.

Copyright, 1926, by the American Medical Association

Archives of Neurology and Psychiatry

VOLUME 15 JANUARY, 1926 NUMBER 1

NEURON DESTRUCTION IN POSTENCEPHALITIC PARALYSIS AGITANS

A MICROMETRIC STUDY OF THE LENTICULAR REGION AND SUBSTANTIA NIGRA *

J. CHARNLEY McKINLEY, M.D.
MINNEAPOLIS
AND
LAWRENCE R. GOWAN, M.D.
DULUTH

The parkinsonian syndrome following epidemic encephalitis has terminated fatally with sufficient frequency to permit numerous, though scattered, observations on the pathologic picture. The following brief review of the available literature will serve to indicate the differences of opinion which exist, relative particularly to the rôle of the globus pallidus or substantia nigra lesions in the production of the syndrome. Lesions in the substantia nigra have been admitted by proponents of the idea that globus pallidus involvement is the essential feature of the pathogenesis of the disease and, conversely, globus pallidus lesions have been described by most of the observers who would place the seat of the difficulty in the substantia nigra. Up to the present no one has undertaken a detailed evaluation of the quantitative amount of cell destruction in these regions in any case. The purpose of this paper is to present the findings of such a study in our three available cases.

The studies of Manschot,[1] Jelgersma,[2] Lewy,[3] and Auer and McGouch [4] placed the pathology of paralysis agitans in the basal ganglia

* From the Division of Nervous and Mental Diseases, University of Minnesota Medical School.

1. Manschot, quoted by Hunt, J. R.: Paralysis agitans, Amsterdam, F. van Rossen, 1904.

2. Jelgersma: Neue anatomische Befunde bei Paralysis agitans und bei chronischer Chorea, Neurol. Centralbl. **27**:995, 1908.

3. Lewy, F. H.: Paralysis agitans, Lewandowsky's Handbuch der Neurologie **2**:920, 1912.

4. Auer, E. M., and McGouch, G. P.: Pathological Findings in Two Cases of Paralysis Agitans, J. Nerv. & Ment. Dis. **43**:532, 1916.

and ansa lenticularis. Their work and that of Wilson,[5] who pioneered in the anatomy and physiology of the striate region, stimulated Hunt[6] to a detailed study of a case of juvenile paralysis agitans. He concluded that the pathologic condition is characterized by selective atrophy of the motor cells of the pallidal system. He described these cells as large motor cells of "the globus pallidus type" which are the "chief cellular content of the globus pallidus" and are also found in "considerable number in the caudate nucleus and putamen." Since the completion of this work, König,[7] the Vogts,[8] Lhermitte and Cornil,[9] Francais and Lhermitte,[10] and Lhermitte, Kraus and McAlpine[11] have reported cases in which pathologic changes occurred in the globus pallidus. These investigators described the lesion as consisting of an atrophy with subsequent diminution in the number of motor cells.

A second belief is that the lesion in paralysis agitans is situated in the substantia nigra and that the occasional disturbances in the globus pallidus may be secondary to those of this region or are merely incidental findings. The following writers have described cases tending to support this theory: Beschet,[12] Mendel,[13] Marinesco and Blocq,[14]

---

5. Wilson, S. A. K.: An Experimental Research Into the Anatomy and Physiology of the Corpus Striatum, Brain **36**:427, 1914.

6. Hunt, J. R.: Primary Atrophy of the Pallidal System of the Corpus Striatum. A Contribution to the Nature and Pathology of Paralysis Agitans, Arch. Int. Med. **22**:647, 1918.

7. König, O.: Beitrag zur Kenntnis der sog. Paralysis agitans sine agitatione auf dem pathologisch-anatomischen Boden der Encephalitis epidemica, Ztschr. f. d. ges. Neurol. u. Psychiat. **75**:221, 1922.

8. Vogt C. and O.: Allgemeinere Ergebnisse unsere Hirnforschung J. f. Psychol. u. Neurol., Leipzig **25**: 1919; Zur Lehre der Erkrankungen des striären System, J. f. Psychol. u. Neurol., Leipzig **25**:631, 1920.

9. Lhermitte, J., and Cornil, L.: Recherches anatomiques sur la maladie de Parkinson, Rev. neurol., June, 1921, p. 587.

10. Francais, H., and Lhermitte, J.: Étude anatomo-clinique d'un cas de syndrome pallidal consécutif d'une encephalite léthargique, Rev. neurol., April, 1922, p. 462.

11. Lhermitte, J.; Kraus, W. M., and McAlpine, D.: Occurrence of Abnormal Deposits of Iron in the Brain in Parkinsonianism, J. Neurol. and Psychopath. **5**:195, 1924.

12. Beschet, quoted by Trétiakoff: Thèse, Paris, 1911.

13. Mendel, quoted by Trétiakoff: Die Paralysis agitans, Berlin, 1911.

14. Marinesco and Blocq, quoted by Trétiakoff: Soc. de Biologia, May 17, 1893.

Trétiakoff,[15] McKinley,[16] Gamno and Omodeii,[17] Foix,[18] Goldstein,[19] McAlpine,[20] Strauss and Globus,[21] Hunt and Cornwall,[22] and Hohman.[23] Trétiakoff [15] cites a case of unilateral paralysis agitans in which the lesion was found in the substantia nigra of the opposite side.

Again, others have found such widespread cerebral involvement that they are unwilling to attribute the condition to a destruction of the substantia nigra or the globus pallidus. Of these, D'Antona and Vegni [24] report a case of paralysis agitans in which lesions were found in the globus pallidus, substantia nigra, dentate nucleus, putamen, internal capsule, thalamus, caudate nucleus and frontal lobe. Hallervorden and Spatz [25] cite a case in which they found localized lesions in the substantia nigra and globus pallidus together with other generalized lesions.

Micrometric methods, consisting of nerve fiber and cell counts, have long been utilized and have proved their value in various anatomic investigations. Rosenthal [26] estimated the number of medullated nerve fibers in different spinal and cerebral nerves of man and determined

---

15. Trétiakoff, C.: Contribution a l'étude de l'anatomie pathologique du locus niger de Soemmering, avec quelques déductions relatives a la pathogenie des troubles du tonus musculaire et de maladie de Parkinson, Thèse, Paris, 1919.

16. McKinley, J. C.: Lesions in the brain of a patient with Postencephalitic Paralysis Agitans, Arch. Neurol. & Psychiat. **9**:47 (Jan.) 1923.

17. Gamno, C., and Omodeii-Jorini, A.: Sulla patogenesi della sindromi amiostatiche postencephalitiche, Pathologica **15**:11, 1923.

18. Foix, C.: Les lésions anatomiques de la maladie de Parkinson, Rev. neurol. **28**:593, 1921.

19. Goldstein, K.: Ueber anatomische Veränderungen (Atrophie der Substantia nigra) bei postencephalitischen Parkinsonismus, Ztschr. f. d. ges. Neurol. u. Psychiat. **76**:627, 1922.

20. McAlpine, D.: The Pathology of the Parkinsonian Syndrome Following Encephalitis Lethargica, with a Note on the Occurrence of Calcification in This Disease, Brain **46**:255, 1923.

21. Strauss, J. H., and Globus, I.: A Contribution to the Neuropathology of the Parkinson Syndrome Following Epidemic Encephalitis, Tr. Am. Neurol. A., 1923, p. 329.

22. Hunt, E. L., and Cornwall, L. H.: The Postencephalitic Parkinsonian Syndrome, J. A. M. A. **84**:29 (Jan. 3) 1925.

23. Hohman, L. B.: Pathologisch-anatomische Untersuchungen über den encephalitischen Parkinsonismus, Arb. a. d. neurol. Inst. a. d. Wiener Univ. **27**:1, 1925.

24. D'Antona, S., and Vegni, R.: Reperto anatomopatologico in un caso di encephalite epidemica cronica, Policlinico, Rome **29**:81, 1922.

25. Hallervorden, J., and Spatz, H.: Eigenartige Erkrankung im extrapyramidalen System mit besonderer Beteiligung des Globus pallidus und der Substantia nigra, Ztschr. f. d. ges. Neurol. u. Psychiat. **79**:254, 1922.

26. Rosenthal, D., quoted by Ingebert: De numero atque mensura elementarium systematis cerebrospinalis symbolae, Diss. Vratislaviae, 1845.

their area in cross section. Stillwig,[27] Tergast,[28] Krause,[29] and Kuhnt [30] have reported similar observations. Birge [31] counted the number of myelinated fibers in the anterior and posterior spinal rootlets and the cells in the anterior horn of the cord. Gaule and Lewin [32] investigated the sacral nerves of rabbits and found an excess of fibers to the distal side of the spinal ganglion. Bühler [33] studied the number of fibers in the ninth spinal nerve of the frog. Thompson,[34] working with Hammerberg's data, estimated the total number of functional nerve cells in the cerebral cortex of adult man to be approximately nine thousand two hundred million. Hardesty [35] counted the number of fibers contained in the dorsal and ventral roots and in the nerve trunk and dorsal branches of spinal nerves in the frog. Dale [36] compared numerically the centripetal and centrifugal medullated nerve fibers arising in the spinal ganglia of the mammal. Dunn [37] made a series of studies on the influence of age, sex and weight on the number of myelinated fibers and the dimensions of the largest myelinated fibers in the ventral root of the second cervical nerve of the white rat. She also determined the number and size of the nerve fibers innervating the skin and muscles of the thigh in the frog. Ingebert [38] enumerated the medullated nerve fibers in the ventral roots of the spinal nerves in

27. Stillwig, B., quoted by Ingebert: Neue Untersuchungen über dem Bau des Rückenmarkes, 1859.

28. Tergast, P.: Ueber das Verhältnis von Nerve und Muskel, Arch. f. mikr. Anat., Bonn **9**:26, 1872.

29. Krause, W.: Handbuch der Anatomie des Menschen, Hannover, 1905.

30. Kuhnt, H.: Zur Kenntnis des Sehnerven und der Netzhaut, Arch. f. Ophth. **25**:179, 1879.

31. Birge, E. A.: Die Zahl der Nervenfasern und der motorischen Ganglienzellen im Rückenmark des Frosches, Arch. f. Physiol., 1882, p. 435.

32. Gaule and Lewin: Ueber die Zahlen der Nervenfasern und Ganglienzellen in Spinalganglien des Kaninchens, Centralbl. f. Physiol. **10**:437, 1896.

33. Bühler, quoted by Hardesty: Untersuchungen über dem Bau der Nervenzellen, Verhandl. d. physik. med. Gesellsch. zu Würzburg. N. F. 31.

34. Thompson, H. B.: The Total Number of Functional Cells in the Cerebral Cortex of Man, etc., J. Comp. Neurol. **9**:113, 1899.

35. Hardesty, I.: Number and Arrangements of the Fibers Forming the Spinal Nerves of the Frog, Rana virescens, J. Comp. Neurol. **9**:65, 1899.

36. Dale, J.: On Some Numerical Comparisons of the Centripetal and Centrifugal Medullated Nerve Fibers Arising in the Spinal Ganglia of the Mammal, J. Physiol. (Foster) **25**:196, 1900.

37. Dunn, E. H.: On the Number and on the Relation Between Diameter and Distribution of the Nerve Fibers Innervating the Leg of the Frog, Rana virescens brachycephala, Cope, J. Comp. Neurol. **12**:297, 1902.

38. Ingebert, C. E.: An Enumeration of the Medullated Nerve Fibers in the Dorsal Roots of the Spinal Nerves of Man, J. Comp. Neurol. **13**:53, 1903.

man. Hatai [39] determined the number and size of the spinal ganglion cells and dorsal root fibers in the white rat. Boughten [40] investigated the increase in the number and size of medullated fibers in the oculomotor nerve of the white rat and of the cat at different ages. Ranson [41] studied the numerical relationship of the large and small cells of the spinal ganglia. Holt [42] determined the number of mitral cells in the olfactory bulb of the white rat. Agduhr [43] studied the size and number of neurons in regard to the postembryonic growth and multiplication of nerve cells. Chi Ping [44] counted and measured the large nerve cells in the superior cervical sympathetic ganglion of the albino rat from birth to maturity. Berger [45] made neuron counts in the left and right precentral gyri at the hand center.

These quantitative studies have been of great aid in acquiring definition in some extremely fundamental anatomic concepts. It is difficult to understand why similar work in pathology should have no significance, as is suggested by the Vogts.[8]

MATERIAL AND METHODS

Three brains from cases of postencephalitic paralysis agitans and three normal brains make up the material for this study.

CASE 1.—Normal. The case was that of a man, aged 45, who was killed in an automobile accident. Death was due to fracture of the cervical vertebrae and widespread visceral injuries. Necropsy was performed eight hours after death. The viscera were normal except for the traumas. There was a moderate amount of hemorrhage over the surface of the brain. The brain was normal on microscopic study.

CASE 2.—Normal. The person was a negro, aged 26, who died of a gunshot wound of the chest. Necropsy was performed six hours after death. There were no other lesions than perforation of the lung, and intrathoracic hemorrhage. The brain was normal grossly and microscopically.

---

39. Hatai, S.: Number and Size of the Spinal Ganglion Cells and Dorsal Root Fibers in the White Rat at Different Ages, J. Comp. Neurol. **12**:107, 1902.

40. Boughten, J. H.: The Increase in the Number and Size of the Medullated Fibers in the Oculomotor Nerve of the White Rat and of the Cat at Different Ages, J. Comp. Neurol. **16**:153, 1906.

41. Ranson, S. A.: Structure of the Spinal Ganglia and of Spinal Nerves, J. Comp. Neurol. **22**:159, 1912.

42. Holt, C. M.: Studies on the Olfactory Bulbs of the Albino Rat, J. Comp. Neurol. **27**:201, 1917.

43. Agduhr, E.: Is the Postembryonic Growth of the Nervous System Due Only to an Increase in Size or Also to an Increase in Number of Neurons? Vers. d. Vergad. d. kon. Acad. v. wet. (afd. Wis-en Naturwk.) **27**:1011, 1919.

44. Chi Ping: On the Growth of the Largest Nerve Cells in the Superior Cervical Sympathetic Ganglion of the Albino Rat from Birth to Maturity, J. Comp. Neurol. **33**:281, 1921.

45. Berger, H.: Untersuchungen über den Zellgehalt der menschlichen Grosshirnrinde, Ztschr. f. d. ges. Neurol. u. Psychiat. **69**:46, 1921.

Case 3.—Normal. This man, aged 35, was killed in an automobile accident. At necropsy it was determined that death was due to fracture and edema of the larynx. The thoracic and abdominal viscera were normal. The brain was normal grossly and microscopically. Necropsy was performed less than twelve hours after death.

Case 4.—Postencephalitic paralysis agitans. The clinical and pathologic findings in this case have been previously reported by one of us.[16]

Case 5.—Postencephalitic paralysis agitans. The patient was a railroad man, aged 27, who was admitted to a hospital in Glendive, Mont., Feb. 18, 1923, complaining of general malaise, headache and pains in the back and in the legs. His temperature at the time was 100 F. Shortly before admission he became confused and irrational. No record of the physical examination in Glendive is available. During the first few days in the hospital the patient was confused, and he did not sleep. A little later, twitching of the face and tremor of the arms developed. One week after admission he became stuporous and slept almost constantly from February 25 to March 11. He could be aroused but would soon fall asleep again. He complained of pain in the back of the neck and of poor vision. He perspired freely. By March 18, 1923, his vision had greatly improved, and the mental symptoms had practically disappeared, so he was allowed to go home. Shortly after returning home he developed a parkinsonian syndrome, was morose, drowsy and weak and complained of dizziness. He grew steadily worse, was readmitted to the hospital in Glendive, and was transferred to the Northern Pacific Brotherhood Hospital in St. Paul, Aug. 5, 1923.

Physical examination at the Northern Pacific Hospital showed a moderately well developed, poorly nourished man. The tonsils were enlarged. Marked pyorrhea alveolaris was present. Heart, lungs and abdomen were normal. The pupils were sluggish. The deep reflexes were hyperactive. There was a masklike expression to the face and a twitching of the jaw. Generalized muscular rigidity was present. The Romberg and Babinski signs were negative. The blood pressure was systolic 110, diastolic 64. The leukocyte count was normal. The blood Wassermann reaction was negative. The urine showed a slight trace of albumin and a few pus cells.

The neurologic condition did not progress during residence at the hospital. The patient was markedly depressed emotionally. On August 26 he secured a piece of cord and committed suicide by hanging himself from an electric light fixture in the bathroom.

Necropsy, performed sixteen hours after death revealed fracture and distortion of the cricoid cartilage, abrasion of the neck and congestion of the kidneys. The scalp and calvarium were normal. The pia-arachnoid over the frontal area showed a few thickened opaque patches. The brain did not appear congested, so death evidently occurred from suffocation rather than from interference with the cerebral circulation. The spinal cord was not removed.

Microscopic examination of the brain revealed scattered fibrotic patches in the meninges over the cortex and especially over the frontal lobes. A few lymphocytes were observed in the meninges. The cortex showed mild scrattered vascular sclerosis and occasional areas of perivascular gliosis. There was no evident reduction in the neuron content. Essentially the same picture was found in the globus pallidus, putamen, pons, medulla and cerebellum. The globus pallidus and putamen contained scattered perivascular round cell infiltrations. The nerve cells in these regions did not appear to be disintegrating.

The substantia nigra presented marked loss of cells. Many of the remaining cells were chromatolytic. There was pronounced perivascular infiltration of lymphocytes and phagocytic cells, with piling up of pigment around the vessels. There was a definite increase in glial tissue running throughout the nucleus, forming a band, the narrowing of which apparently accentuated the amount of cell débris found in the zona compacta.

CASE 6.—Postencephalitic paralysis agitans. The case is that of a man, aged 21, who was admitted to the Minneapolis General Hospital, June 1, 1923, complaining of partial paralysis of the left arm and right leg, persistent tremor of the left hand and arm and of the tongue, and inability to close the mouth and eyelids. In February, 1920, he had an attack of "influenza." He kept on working but complained of being very tired. On March 2, 1921, he developed severe headache and tremor of the left arm and face. He became irrational and violent. He was unconscious for five days. Following this acute episode he became fairly well, but the headache and tremor of the left arm and face persisted. The severe headache lasted for one and one half years. The tremor became progressively worse and affected the right leg also. Dysphagia and dysarthria were present during the last year of the patient's life.

Examination on admission to the hospital disclosed a classic picture of paralysis agitans: a marked masklike expression, rhythmic tremor of the left hand and tongue, mouth wide open and marked spasticity of all the extremities. The heart and lungs were normal. The abdominal examination was negative. Blood pressure was systolic 118, diastolic 70. The pupils were about equal, slightly irregular and reacted promptly to light. There was extreme difficulty in closing the jaws. The deep reflexes were normal on the right and increased on the left. The cremasteric and abdominal reflexes were normal on the right and hyperactive on the left (?). The plantar reflexes were normal bilaterally. There was a suggestive ankle clonus on the left, no clonus on the right. Sensation was normal. The voice was weak and high pitched. The leukocyte count was normal. The blood Wassermann test was negative. Urine analysis was negative. The spinal fluid was negative as to cell count, globulin, colloidal gold and Wassermann reactions. There was little change in the condition of the patient until shortly before death, when he developed increasing difficulty in moving his jaw. He was hardly able to swallow. He became steadily weaker and died, Sept. 10, 1923.

Necropsy was performed six hours after death. Terminal bronchopneumonia was found. The brain appeared normal on gross examination except for loss of pigment in the substantia nigra.

Microscopic examination of the brain revealed little abnormality in the cortex, putamen, globus pallidus, pons, medulla or cerebellum, except very mild vascular scleroses with here and there a little glial increase and an occasional area of slight perivascular round cell infiltration. The substantia nigra was profoundly altered. Here there was evidence of considerable cell destruction and loss. Many of the cells were atrophied, giving them an appearance of increased pigmentation. Much free pigment, numerous mononuclear phagocytic cells and plasma cells were found around the vessels. There was a decided increase in glial tissue throughout the region.

The brains from the foregoing cases were fixed and preserved in solution of formaldehyde (4 per cent). In Case 4 the brain was placed in the fluid in toto; in the remaining cases, the fixative was injected into the vessels at the base.

In selecting the areas to be studied, serial blocks were cut on either side through the lenticular region, midbrain and pons. Spatial orientation of the sections was retained throughout the study. Sections eight microns thick, from the dorsal or inferior side of each block, were prepared by the paraffin method and stained with thionin.

In Case 3 the total number of globus pallidus and putamen nerve cells was determined in one section from each of five serial blocks through the region. From an inspection of these data it appeared reasonable to accept a block passing approximately through the center of the globus pallidus and putamen as representative of the nuclei. In all the other cases the data collected are from such a block. A similar study was made of the substantia nigra region of Case 1. The level selected for this nucleus was that passing from the origin of the third nerve on the brain surface to the boundary between the superior and inferior corpora quadrigemina.

In accordance with the foregoing determinations, twenty serial sections were made from the representative block of the lenticular region, and ten sections of the substantia nigra region of each of the other cases studied. Owing to the fact that the greater part of the material in Case 4 had already been used in a previous study,[16] only seven slides were obtained from the substantia nigra area in this case.

The area of the slide to be counted was determined under a binocular dissecting microscope, and outlined in India ink on the cover slip. The boundaries of the putamen and globus pallidus were recognized by their respective cell topography. The limits of the substantia nigra were located as follows: A line was drawn between the substantia nigra and the nucleus ruber, another line was drawn ventral to the substantia nigra so that all cells, pigmented or not pigmented, which appeared to belong to the nucleus, were included between the two lines. The lateral and medial extremities of these lines were then connected and the irregular rectangle thus formed represented the area of the substantia nigra.

The neuron counting was done by means of a Whipple's eyepiece micrometer disk, which was previously standardized against a stage micrometer scale. The exact area in millimeters of the micrometer field for any lens combination at a given tube length was thus determined. Trial counts were made with different lenses, and the 8 mm. objective, and the 10 × ocular at a tube length of 60 mm., actual magnification approximately 200 diameters, were selected as most satisfactory. This set-up provided the largest possible field which would give a sufficient magnification to prevent omissions of cells. The relatively high magnification was necessary because no cells were counted which did not contain nucleoli.

In the putamen every sixth field was counted. It was determined from the putamen of Case 3, in which the sections were counted entire,

that every sixth field gave a fair sample of a single slide, and permitted the examination of six sections with no more effort than that consumed in counting all the fields in one slide. In the globus pallidus and substantia nigra the total area outlined on each slide was counted because of the relatively small number of cells. In the putamen and substantia nigra each square millimeter was taken as a single observation, but in the globus pallidus an area of 10 sq. mm. was recorded as a single observation. Orientation was maintained by means of a mechanical stage.

The accuracy of the individual counts may be illustrated by the following examples. One of us counted the neurons in the globus

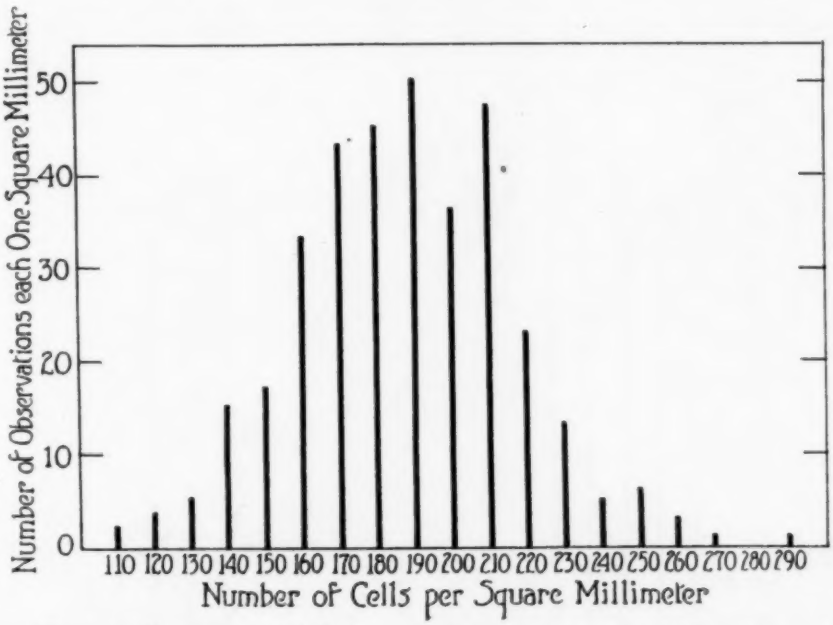

Number of Observations each One Square Millimeter
0
10
20
30
40
50
110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290
Number of Cells per Square Millimeter

Chart 1.—Frequency distribution of the count in the right putamen in Case 3, normal. Compare with Table 1 for numerical values referring to this count.

pallidus in Case 5, slide 13, and obtained an average of 75.8 cells per ten square millimeters. The other counted the same slide and found 74.1 cells per ten square millimeters, a difference of only 1.7 cells per ten square millimeters. Case 5, slide 1, globus pallidus, was tested in the same way. In this slide the counts were 73 and 73.75 cells per ten square millimeters, respectively, a difference of 0.75 cells per ten square millimeters. Another count was made in the same region of this slide with a 4 mm. objective and 20 × ocular, at a magnification of approximately 880 diameters so as to obtain practically absolute accuracy in the recognition of nucleoli, with the satisfactory result that

73.5 cells per ten square millimeters were found. Further checking of a similar nature was done when any uncertainty arose, so we are satisfied that no gross discrepancies of judgment have entered into the data collected.

During the counting process, after having acquired thorough familiarity with the averages to be expected, we repeatedly estimated

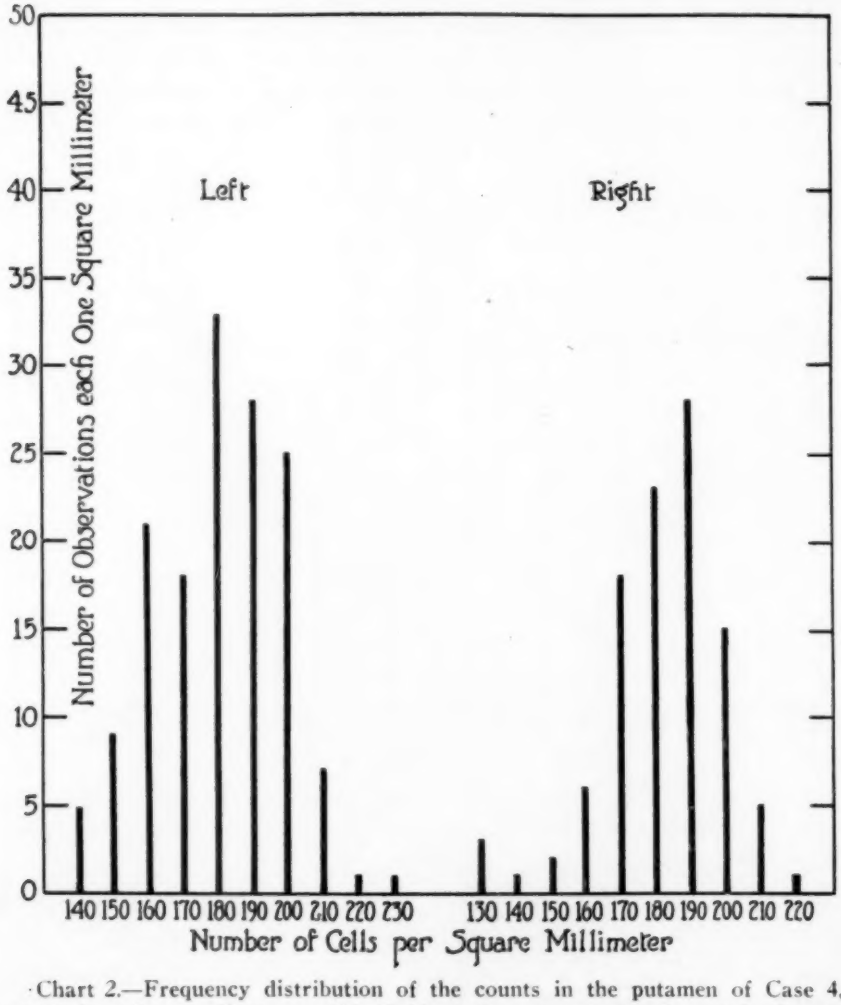


Chart 2.—Frequency distribution of the counts in the putamen of Case 4, paralysis agitans. Compare with Table 1 for numerical values referring to these counts.

by inspection the number of cells in a unit area, and commonly found differences between the estimate and the actual count as great as 30 to 40 per cent. It has thus become obvious to us that statements concerning cell loss, based on inspection, however carefully done and

practically regardless of the amount of previous experience even with a single area of the brain, are of little significance unless the decrease is extremely marked.

TREATMENT OF DATA

In order to come to definite conclusions in a study of this sort, it is necessary to apply certain of the more elementary statistical methods

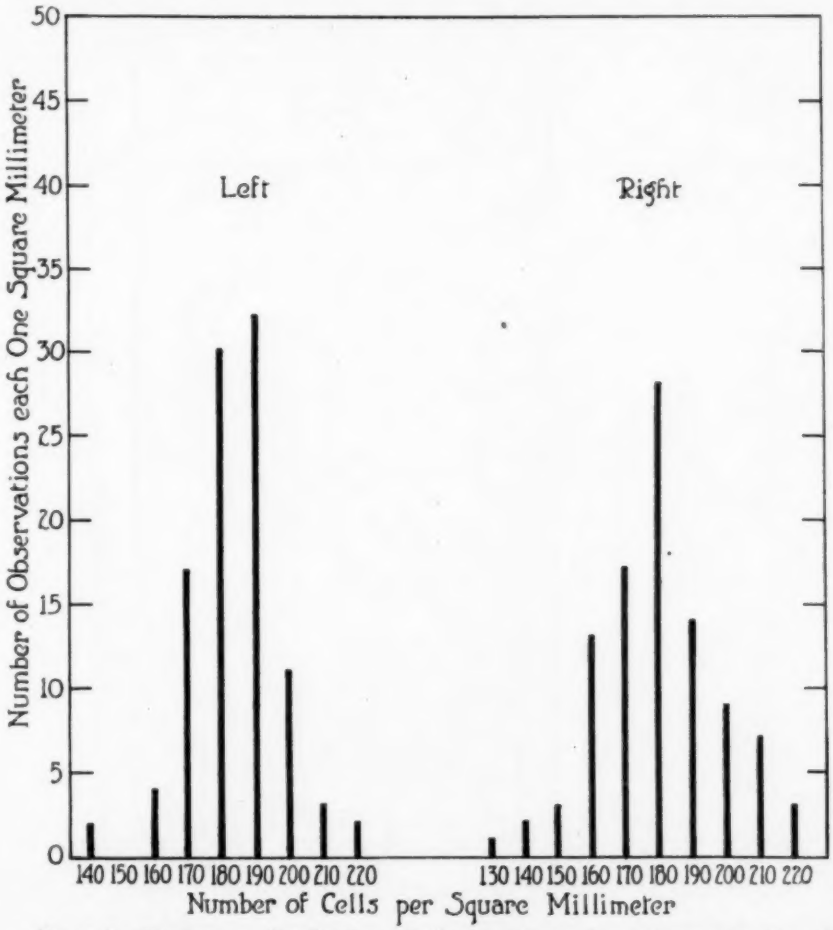


Chart 3.—Frequency distribution of the counts in the putamen in Case 5, paralysis agitans. Compare with Table 1 for numerical values referring to these counts.

to the data collected. Though these methods have been fully developed in numerous treatises on statistics,[46] a short explanation of those

46. The following books have been freely consulted in the preparation of the present data: Jones, D. C.: A First Course in Statistics, Ed. 2, London, G. Bell and Sons Ltd., 1924. King, W. I.: The Elements of Statistical Method, New York, The Macmillan Company, 1912. Bowley, A. L.: Elements of Statistics, Ed. 4, New York, Charles Scribner's Sons, 1920.

used in this paper will probably be welcomed by readers whose work has not led them into this field.

The central tendency of each count was determined by calculation of the familiar average or arithmetic mean. Dispersion of the items about this central tendency was obtained by calculation of the standard deviation and probable error (Tables 1, 2 and 3).

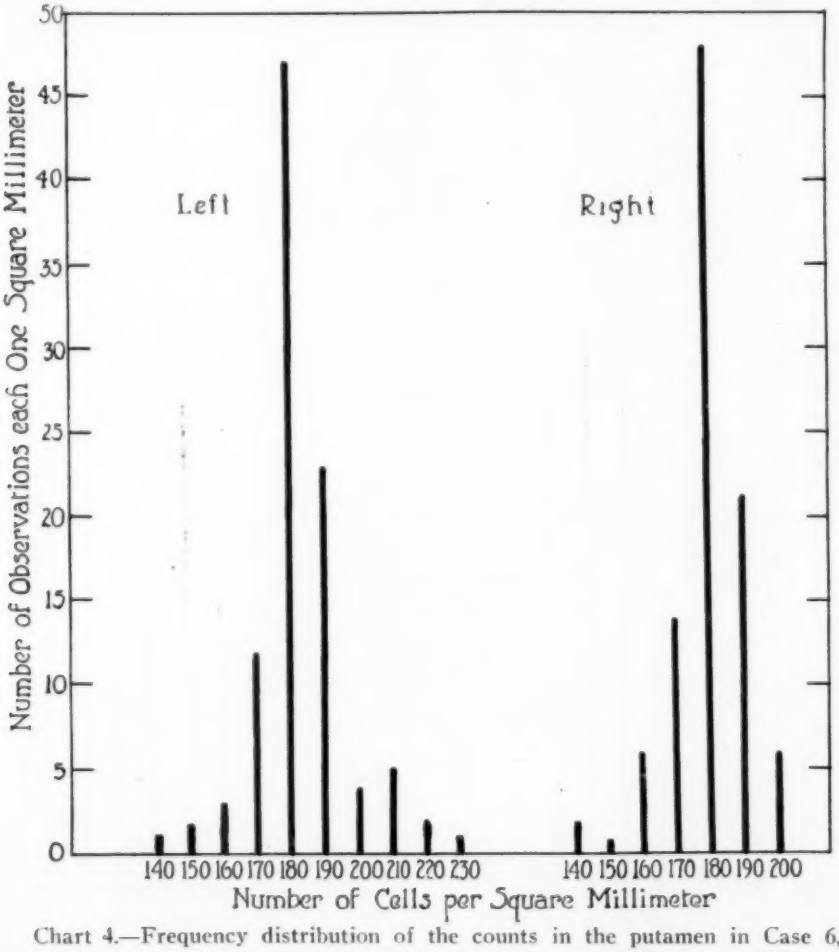


Chart 4.—Frequency distribution of the counts in the putamen in Case 6, paralysis agitans. Compare with Table 1 for numerical values referring to these counts.

The standard deviation is commonly expressed by the formula

$$\sigma = \sqrt{\frac{\Sigma d^2}{n}}$$

in which σ is the standard deviation, Σd^2 is the sum of the squares of the deviations from the average, and n is the number of items in the series.

If the standard deviation is added to and subtracted from the average of the series, limits of dispersion about the average are determined outside of which or within which there is about an equal chance that any small sample taken from the series will fall. For instance, in Table 1, Case 3, the average in the putamen is 186.9 cells per square millimeter and the standard deviation is 28.7 cells per square millimeter. Adding and subtracting,

$$186.9 + 28.7 = 215.6$$
$$186.9 - 28.7 = 158.2$$

If now 1 sq. mm. should be counted in one of the slides from which these figures have been obtianed, there would be about an

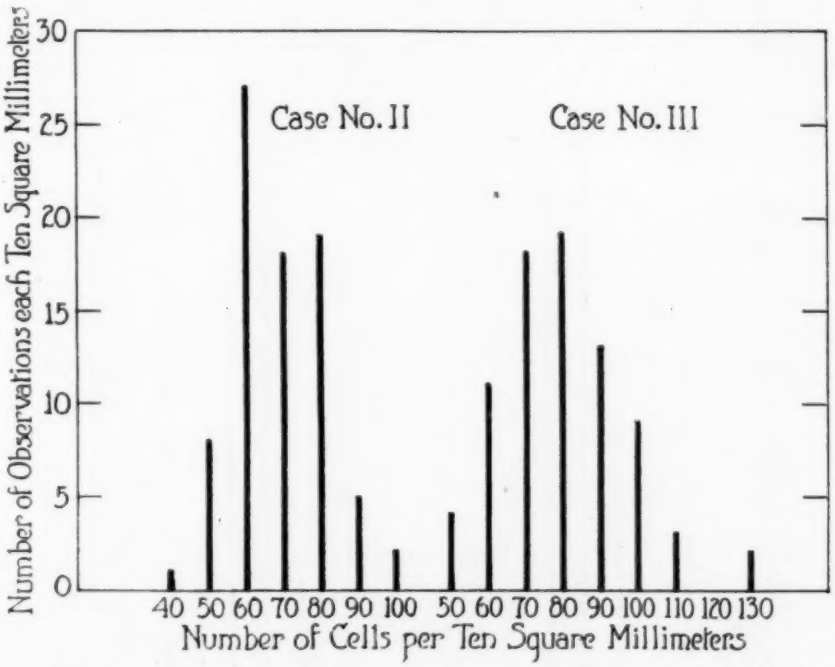


Chart 5.—Frequency distribution of the counts in the globus pallidus in Cases 2 and 3, normal. Compare with Table 2 for numerical values referring to these counts.

equal chance that the number of cells contained in the millimeter would be inside or outside of the limits of 158.2 to 215.6. The count would not, under any circumstances, be smaller or larger in this imaginary square millimeter than the extreme range for the series of 111 to 287 cells.

The probable error is obtained by multiplying the standard deviation by 0.6745. In the case just mentioned the probable error is $0.6745 \times 28.7 = 19.1$. This number added to or subtracted from the average of 186.9 cells per square millimeter establishes the limits of the

probable range of variability as 167.8 to 206.0. This means that the number of cells in our imaginary millimeter would probably vary from the average of the whole series (186.9) by as much as 19.1. On the other hand, if a fair number of such millimeters were to be counted from the sections in this series (a small series of 100 to 150 sq. mm., for instance), the individual variations from the true average would

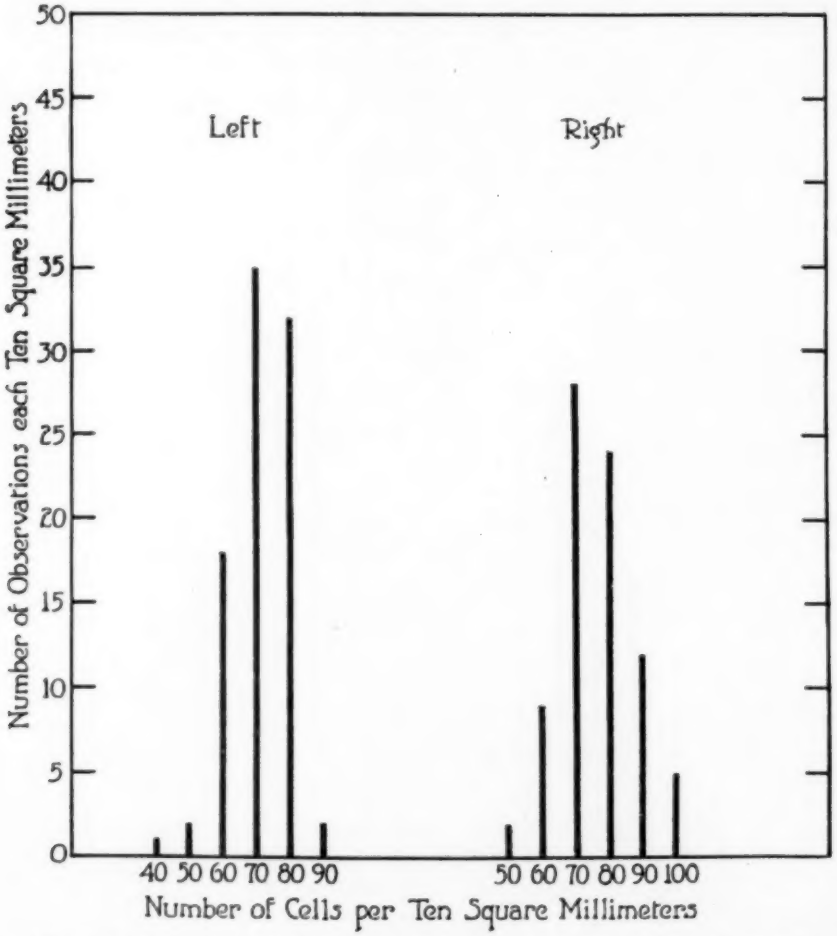


Chart 6.—Frequency distribution of the counts in the globus pallidus in Case 4, paralysis agitans. Compare with Table 2 for numerical values referring to these counts.

tend to offset one another so that the average of the small series would very likely fall within the probable range of variability of the whole series.

From the foregoing, because of the wide spread of the frequency distributions, it is evident that some measure of the significance of the

differences of the averages of the sample distributions in the several series of counts, especially in comparing the abnormal with the normal cases, is desirable. Such a measure has been developed and is expressed by the formula:

$$\frac{a_1 - a_2}{0.6745\sqrt{\frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_2}}}$$

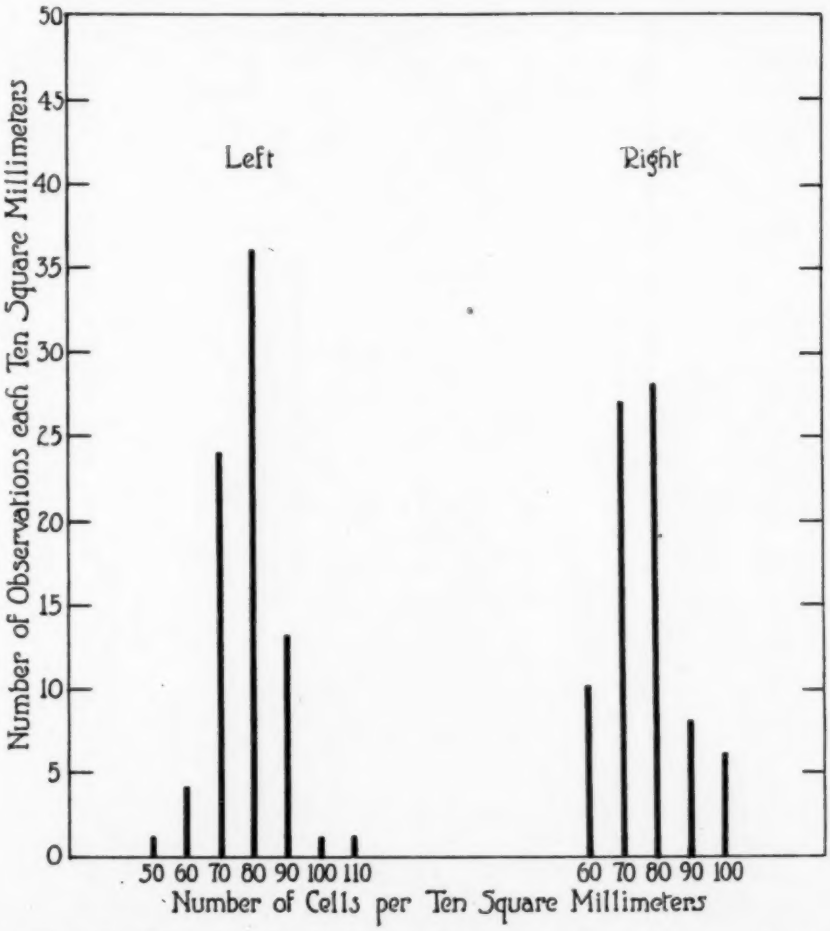


Chart 7.—Frequency distribution of the counts in the globus pallidus in Case 5, paralysis agitans. Compare with Table 2 for numerical values referring to these counts.

in which a_1 indicates the larger of the averages of the two cases compared; a_2, the smaller of the averages of the two cases compared; σ_1^2, the square of the standard deviation of the first of the two cases compared; σ_2^2, the square of the standard deviation of the second of the

two cases compared; n_1, the number of observations of the first of the two cases compared; n_2, the number of observations of the second of the two cases compared.

It has been shown that if the resulting figure, or index, is less than 3, the difference is significant only of those variations which might be

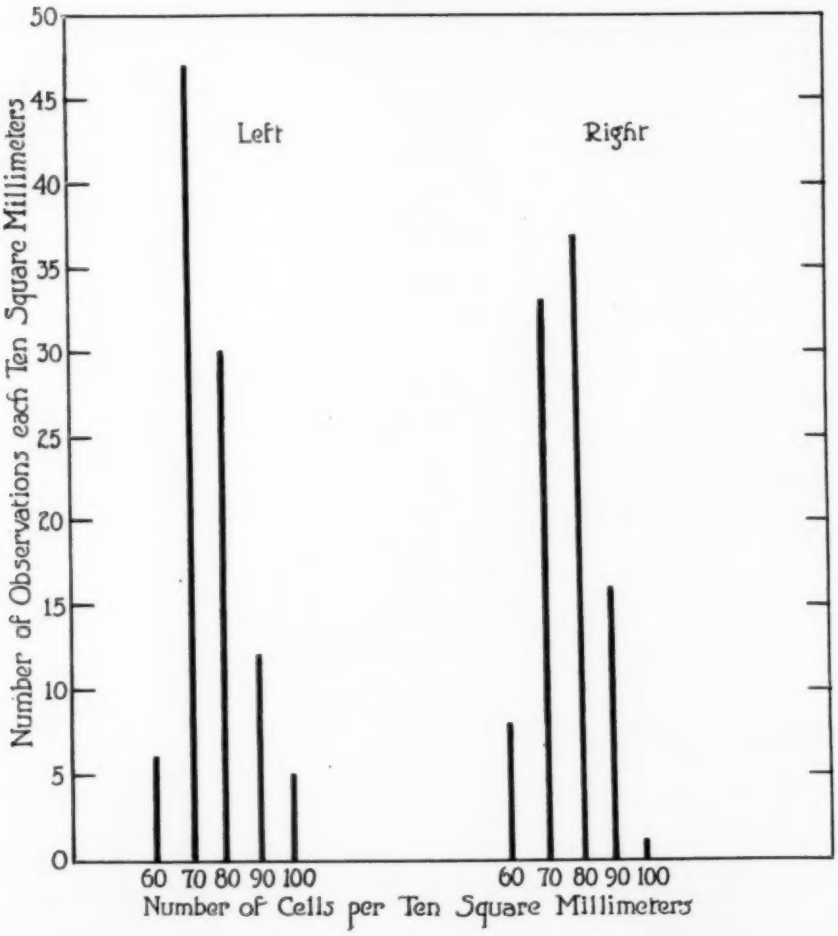


Chart 8.—Frequency distribution of the counts in the globus pallidus in Case 6, paralysis agitans. Compare with Table 2 for numerical values referring to these counts.

expected from the selection of a sample from a uniform distribution. For example: To obtain the index of the significance of the difference in the putamen of Case 3 (normal) and the putamen of Case 4 (paralysis agitans), as shown at the top of Chart 17, and obtaining the averages,

standard deviations and number of observations from Table 1, the calculation is as follows:

$$\frac{a_1 - a_2}{0.6745\sqrt{\frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_2}}} = \frac{186.9 - 180.1}{0.6745\sqrt{\frac{(28.7)^2}{347} + \frac{(18.5)^2}{150}}} = \frac{6.8}{1.44} = 4.7.$$

This represents the index of the significance of the difference of the averages of the sample sections counted in these two cases The indexes of significance of the differences of the several counts are shown numerically and graphically in Chart 17.

Charts 1 to 13 represent the frequency distributions of the various counts. They are reproduced only as an easy method of presenting the original data for the use of those who might be interested from some angle other than that of the present treatment. These thirteen figures are not intended and should not be used for comparison of the counts with one another except roughly. Comparisons between the

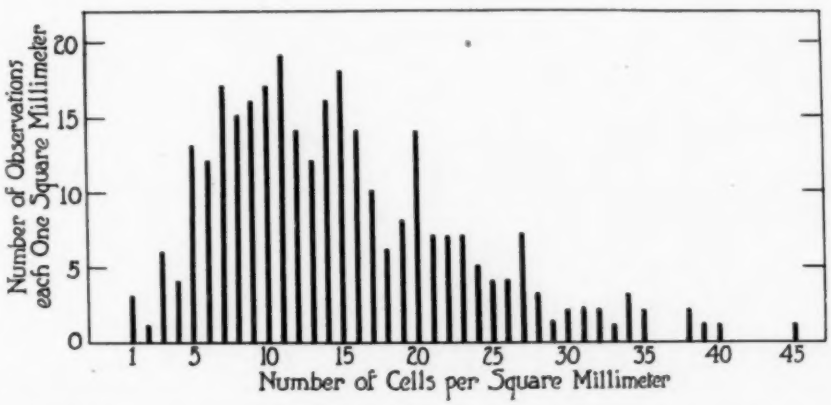


Chart 9.—Frequency distribution of the count in the left substantia nigra in Case 1, normal. Compare with Table 3 for numerical values referring to this count.

distributions of the series are permissible only in percentage frequency charts, such as Charts 14, 15 and 16, or by special methods, such as the computation of the significance of the differences of the averages as shown in Chart 17. The counts of globus pallidus are plotted by tens of cells per ten square millimeters; those of the putamen by tens of cells per one square millimeter. Thus, a line in the globus pallidus charts representing the number of observations at 90 cells per ten square millimeters really includes all counts from 85 to 94 cells per ten square millimeters, inclusive. The averages, standard deviations, probable errors and indexes of the significance of differences are all derived from the original, unmodified data. This mode of charting would doubtless give rise to small discrepancies if one were to recom-

pute the averages, standard deviations, etc., from the data given in the frequency graphs. The charts of the substantia nigra counts all represent the original data without modification.

COMMENT

Certain points of interest may be noted in the accompanying tables. In Table 1 the arithmetic mean for the normal case is 186.9 cells per square millimeter in the putamen. The average of the parkinsonian cases most divergent from the normal is that in Case 6, R, 175.3 cells per square millimeter; but the probable range of variability for the normal

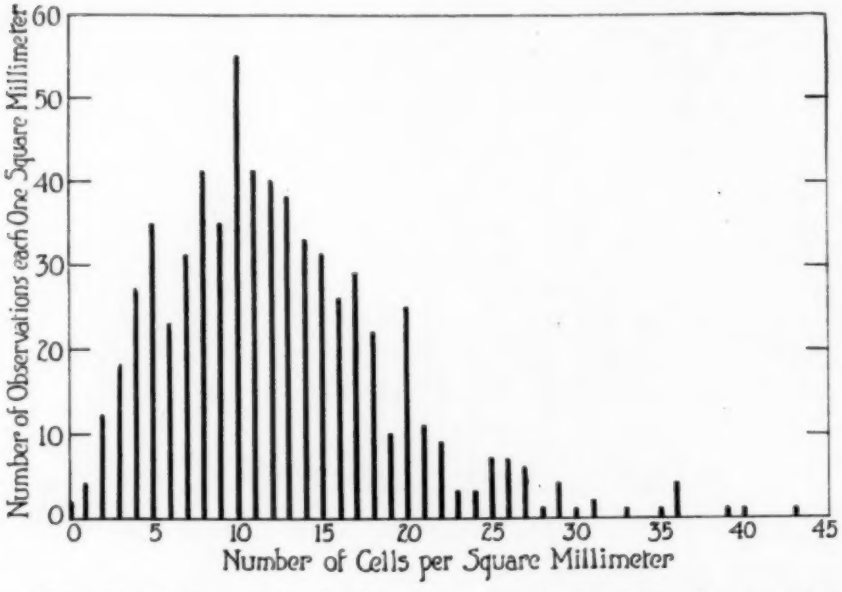


Chart 10.—Frequency distribution of the count in the right substantia nigra in Case 3, normal. Compare with Table 3 for numerical values referring to this count.

case is 167.8 to 206.0 cells per square millimeter and for the abnormal case 168.7 to 181.9—a close correspondence of the two series. Similar comparisons may be made between the other abnormal cases and the normal case in this table, and also for the globus pallidus in Table 2. No evident reduction in the number of cells of the putamen or globus pallidus can be determined on inspection of these two tables.

Table 3 contains the values for the counts in the substantia nigra. The averages of the number of cells per square millimeter in the normal cases are more than twice as great as the largest average of the parkinsonian cases (14.1 and 12 as compared with 5 cells per square

millimeter). In other words, in the pathologic case with the highest count, the cells are reduced in number to $\frac{5.0 \times 100}{12.0} = 41.7$ per cent. of the lower normal, a reduction of $100 - 41.7 = 58.3$ per cent. In the pathologic case with the lowest count compared with the higher normal, the cells are reduced to $\frac{1.8 \times 100}{14.1} = 12.7$ per cent. of the normal, a reduction of $100 - 12.7 = 87.3$ per cent. None of the probable ranges

TABLE 1.—*Numerical Data Referring to the Various Counts in the Putamen*

Case Number Right or Left	No. of Observations Each 1 Sq. Mm.	Total Number Cells Counted	Arithmetic Mean	Standard Deviation	Probable Error	Extreme Range of Variability	Probable Range of Variability	Compare with Chart No.
3, R, Normal.....	347	65,227	186.9	28.7	19.1	111-287	167.8-206.0	1
4, L, Paralysis agitans..	150	27,015	180.1	18.5	12.5	137-234	167.6-192.6	2
4, R, Paralysis agitans..	102	18,451	180.9	16.5	11.1	125-215	169.8-192.0	2
5, L, Paralysis agitans..	100	18,321	183.2	13.3	9.0	138-220	174.2-192.2	3
5, R, Paralysis agitans..	98	17,250	176.0	17.5	11.8	130-223	164.2-187.8	3
6, L, Paralysis agitans..	100	18,264	182.6	13.5	9.1	141-234	173.5-191.7	4
6, R, Paralysis agitans..	100	17,530	175.3	9.8	6.6	138-200	168.7-181.9	4

TABLE 2.—*Numerical Data Referring to the Various Counts in the Globus Pallidus*

Case Number Right or Left	No. of Observations Each 10 Sq. Mm.	Total Number Cells Counted	Arithmetic Mean	Standard Deviation	Probable Error	Extreme Range of Variability	Probable Range of Variability	Compare with Chart No.
2, L, Normal.....	80	5,443	68.0	12.3	8.2	43- 96	59.8-76.2	5
3, R, Normal.....	79	6,217	78.7	17.2	11.6	48-135	67.1-90.3	5
4, L, Paralysis agitans..	90	6,381	70.9	9.0	6.1	44- 87	64.8-77.0	6
4, R, Paralysis agitans..	79	5,926	75.9	10.6	7.1	51- 98	68.8-83.0	6
5, L, Paralysis agitans..	80	6,211	77.6	8.5	5.7	52-105	71.9-83.3	7
5, R, Paralysis agitans..	80	6,115	72.7	10.2	6.9	57-104	65.8-79.6	7
6, L, Paralysis agitans..	100	7,566	75.7	9.1	6.1	58-104	69.6-81.8	8
6, R, Paralysis agitans..	100	7,591	75.9	8.1	5.5	58- 95	70.4-81.4	8

TABLE 3.—*Numerical Data Referring to the Various Counts in the Substantia Nigra*

Case Number Right or Left	No. of Observations Each 1 Sq. Mm.	Total Number Cells Counted	Arithmetic Mean	Standard Deviation	Probable Error	Extreme Range of Variability	Probable Range of Variability	Compare with Chart No.
1, L, Normal.....	297	4,179	14.1	8.0	5.3	1-45	8.8-19.4	9
3, R, Normal.....	641	7,692	12.0	6.8	4.5	0-43	7.5-16.5	10
4, L, Paralysis agitans..	120	221	1.8	1.3	0.9	0- 5	0.9- 2.7	11
4, R, Paralysis agitans..	95	186	2.0	1.4	0.9	0- 6	1.1- 2.9	11
5, L, Paralysis agitans..	391	1,968	5.0	2.6	1.7	0-19	3.3- 6.7	12
5, R, Paralysis agitans..	420	1,851	4.4	2.3	1.6	0-12	2.8- 6.0	12
6, L, Paralysis agitans..	348	1,172	3.4	1.5	1.0	0- 9	2.4- 4.4	13
6, R, Paralysis agitans..	264	806	3.1	1.5	1.0	0- 7	2.1- 4.1	13

of variability in the substantia nigra of the parkinsonian cases overlaps the probable ranges of variability that are normal.

Though averages, standard deviations, probable errors and ranges are necessary for the proper presentation and understanding of these data, the formula for the index of the significance of the difference of the averages of two sample distributions is particularly applicable here.

It has already been noted that if the index is less than 3, the difference is significant only of those variations which might be expected from the selection of a sample from a uniform distribution.

In the upper portion of Chart 17 the indexes of the significance of the differences of the various averages in the putamen are shown.

The putamen was included in this study as an additional check on the method used because of its convenient presence next to the globus

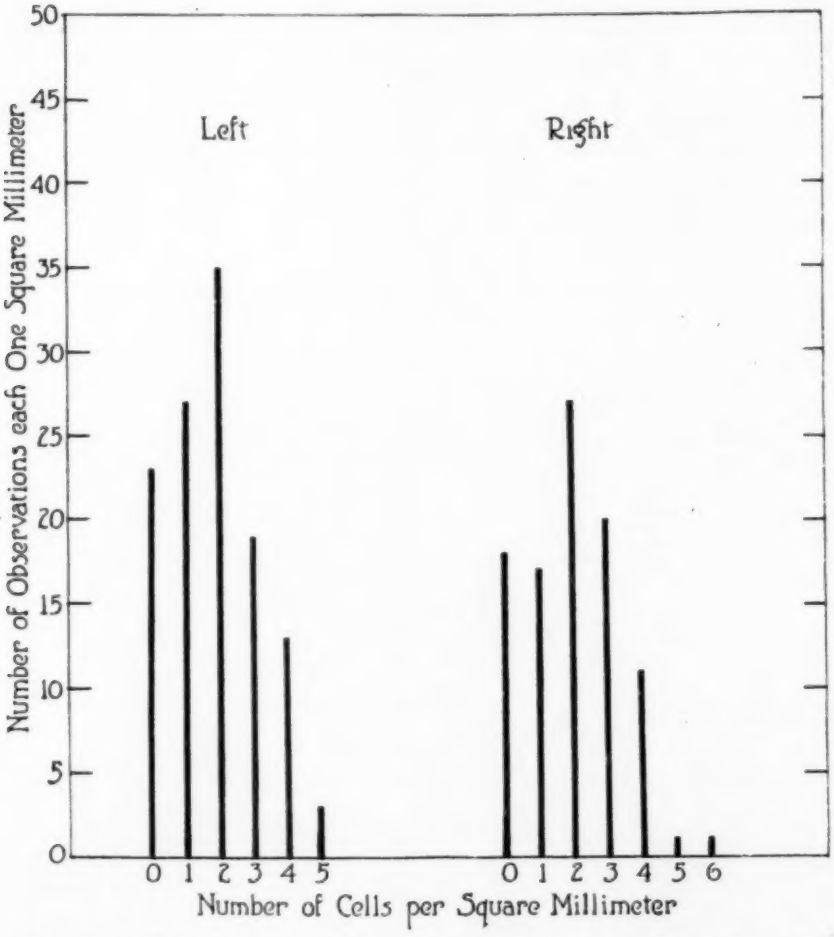


Chart 11.—Frequency distribution of the counts in the substantia nigra in Case 4, paralysis agitans. Compare with Table 3 for numerical values referring to these counts.

pallidus, and more especially because it has not been incriminated as a possible seat of the parkinsonian lesion. This statement must be taken to exclude the large cells of the globus pallidus type which Hunt [6] has described undergoing atrophy and disappearance in paralysis agitans.

These cells occur about one to the square millimeter in all our cases. If they were all gone, they would reduce our counts about one cell per square millimeter, and this would be of no significance in counts averaging around 180 to the millimeter. But they appear to be entirely preserved, so that presumably all the figures for the putamen represent normal counts.

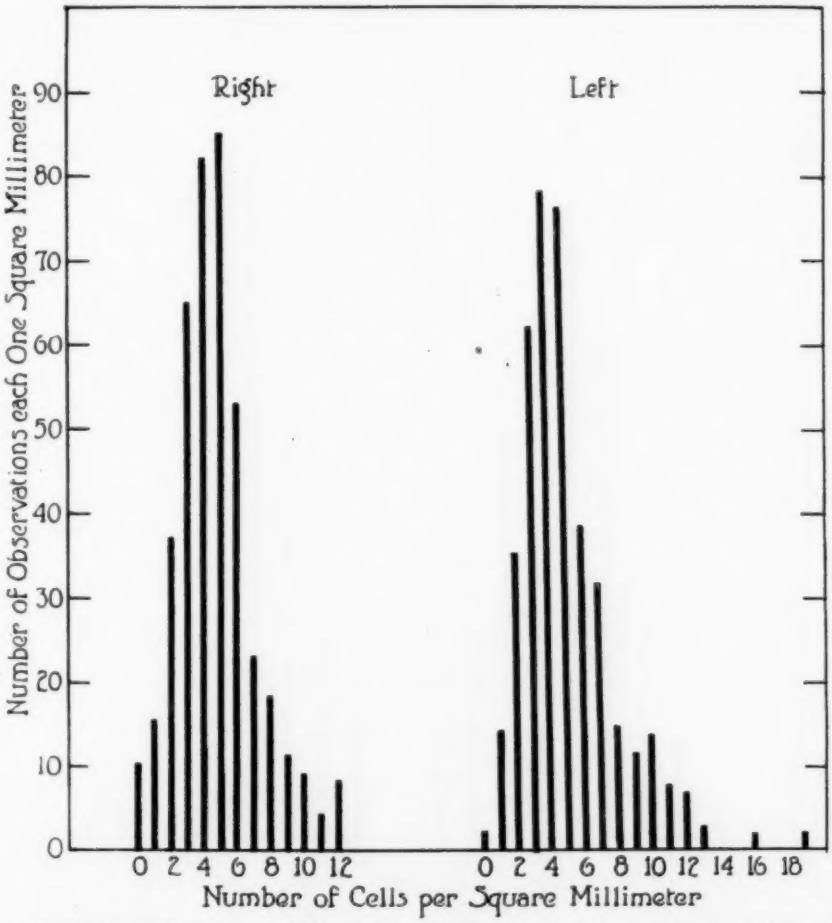


Chart 12.—Frequency distribution of the counts in the substantia nigra in Case 5, paralysis agitans. Compare with Table 3 for numerical values referring to these counts.

However, most of the putamen indexes are greater than 3, so the differences must be significant of more than the method of sampling alone. In all probability, this apparent discrepancy is due in part to slight or moderate irregularities in the cell distribution in different localities of the nucleus. The irregularities are not pronounced, but are present evidently as the result of larger and smaller numbers of medullated

fiber bundles of varying size passing through the area. At least, when fiber bundles are numerous and large, the cell counts are low. Another factor may enter here; there is doubtless a small amount of individual variation from brain to brain, not only in the cell distributions in a given area, but also in the absolute number of cells in that region.

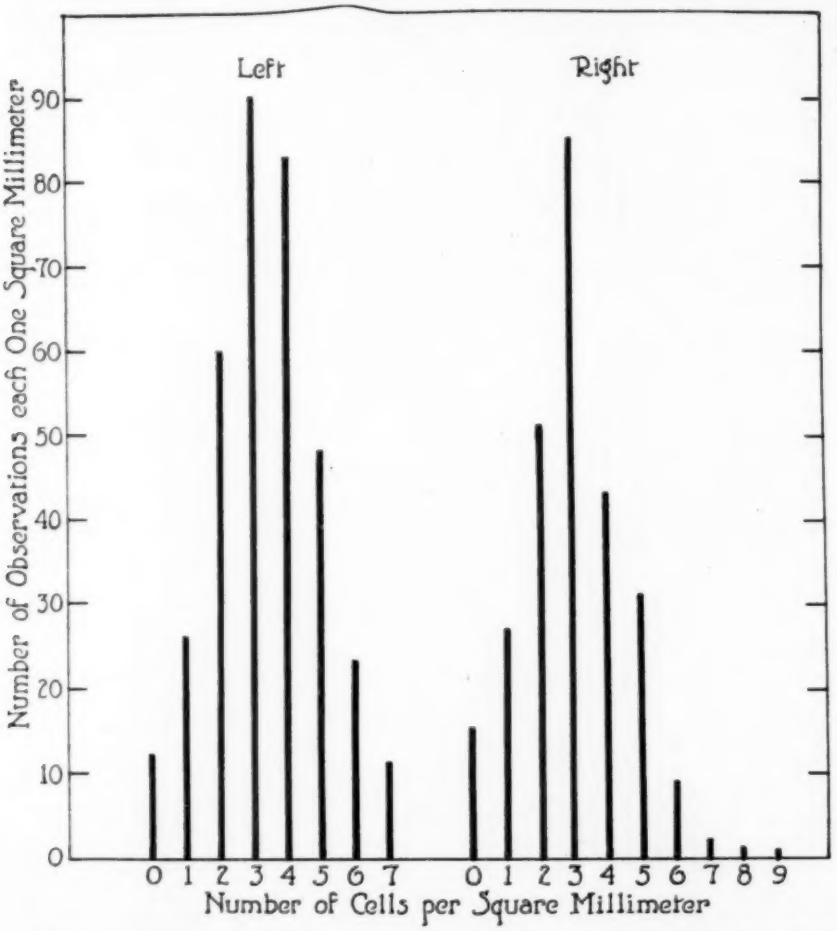


Chart 13.—Frequency distribution of the counts in the substantia nigra in Case 6, paralysis agitans. Compare with Table 3 for numerical values referring to these counts.

Unequal shrinkage in fixation and handling of the tissues probably likewise plays a rôle. We have not attempted to study these points beyond making superficial note of their occurrence. Judging by the indexes, the significance of these factors, though undeniable, is not great.

The middle portion of Chart 17 shows the indexes of the significance of the differences in the globus pallidus samples. The index for the two

normal cases is 6.7. Since the cases are normal, this must be due to irregularities of cell distribution or individual variation or both. The indexes obtained for each normal case compared separately with the right and left sides in the cases of paralysis agitans range from 0.8 to 8.5. In five instances the indexes are less than 3, indicating that the samples have been taken from almost similar if not identical cell distributions. In

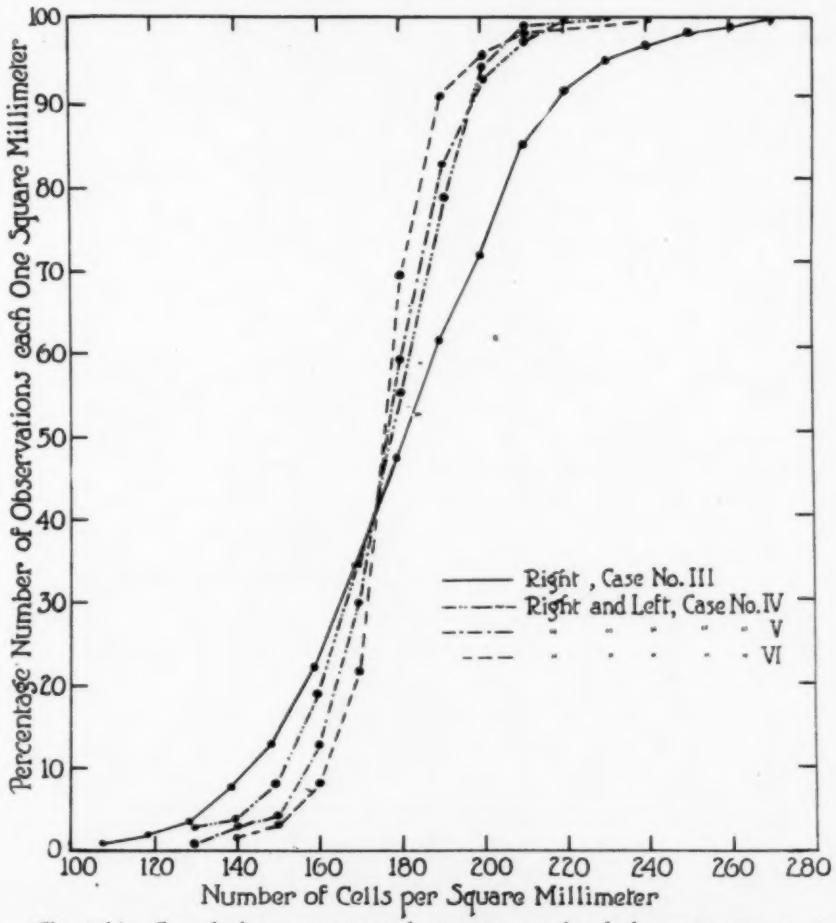


Chart 14.—Cumulative percentage frequency graph of the putamen counts. Case 3 was a normal case, the others were cases of paralysis agitans. The frequency distributions are similar in all cases except for a relatively wide spread in the normal case. Compare with Table 1 for numerical data.

four instances the indexes are less than the index of the normal but more than 3. In three instances they are slightly more than the normal, but here the averages in the parkinsonian cases are larger than that in the normal with which they are compared. The fact that nine of the indexes are lower than that of the normal and only three are higher

would indicate that the differences are due to the same kind of circumstances as those discussed for the putamen. The indexes from the globus pallidus, on the whole, represent no greater differences than are found in the putamen. No cell loss has occurred in the globus pallidus so far as can be determined by the methods used in this study.

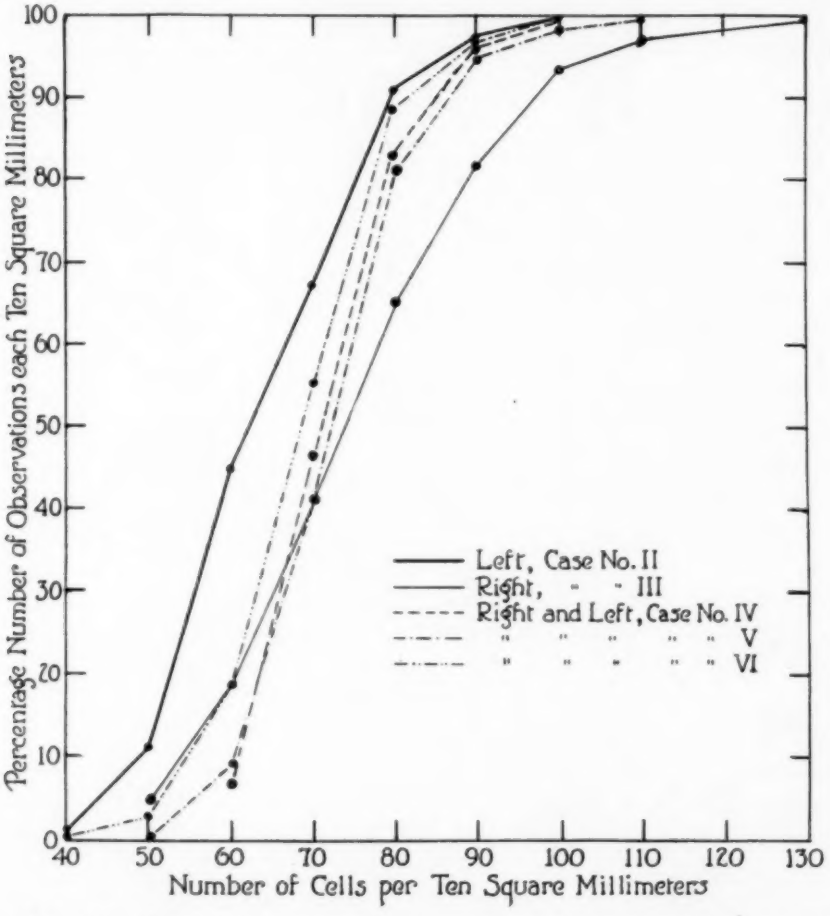


Chart 15.—Cumulative percentage frequency graph of the globus pallidus counts. Cases 2 and 3 were normal, the others were cases of paralysis agitans. The frequency distributions are similar in all cases except that the parkinsonian curves are a little higher than one normal curve and a little lower than the other. Compare with Table 2 for numerical data.

The lowest portion of Chart 17 contains the indexes of the significance of the difference of the various averages obtained in the substantia nigra. The index comparing the two normal cases (Cases 1 and 3) is 5.8. This index is probably due to the factors already mentioned. The indexes for the cases of paralysis agitans, right and left sides compared separately

with each of the normal cases, range from 28.2 to 50.5. These figures, considered with the index of 5.8 in the normal cases, show that there is a difference significant of much more than the foregoing factors. The indexes are much larger than those obtained from the globus pallidus and putamen. Doubtless, the only additional factor entering into this increased difference is that of cell reduction due to the pathologic state.

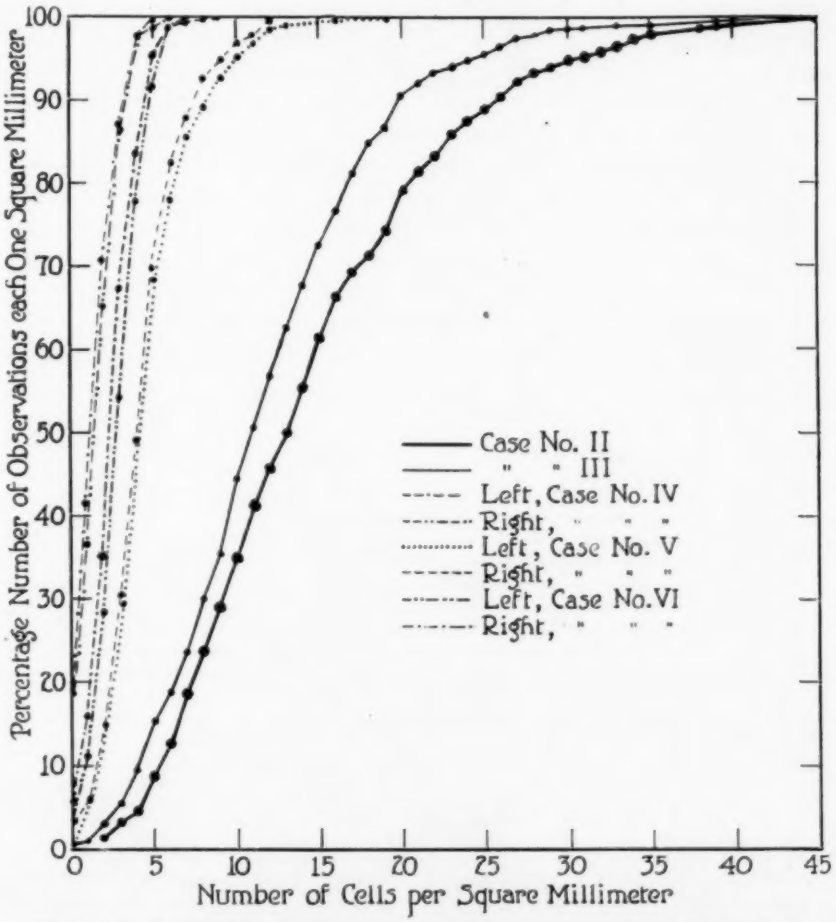


Chart 16.—Cumulative percentage frequency graph of the substantia nigra counts. Cases 2 and 3 were normal cases, the others were cases of paralysis agitans. The distributions of the parkinsonian cases indicate much lower counts than in the normal cases. Compare with Table 3 for numerical data.

Another point of interest regarding the substantia nigra may be observed from the data presented. The frequency distributions of the normal cases are almost similar (Charts 9 and 10). They are markedly skewed to the right. This is evidently due to the few areas of great

cell concentration in the zona compacta. The majority of the millimeters counted in the normal cases contain up to 18 or 20 cells per square millimeter. These predominant low counts result from counting the scattered cells of the zona reticularis. Of the parkinsonian cases, only Case 5 (Chart 12) shows any definite tendency toward skewness. In other words, in Cases 4 and 6, the zona compacta has practically

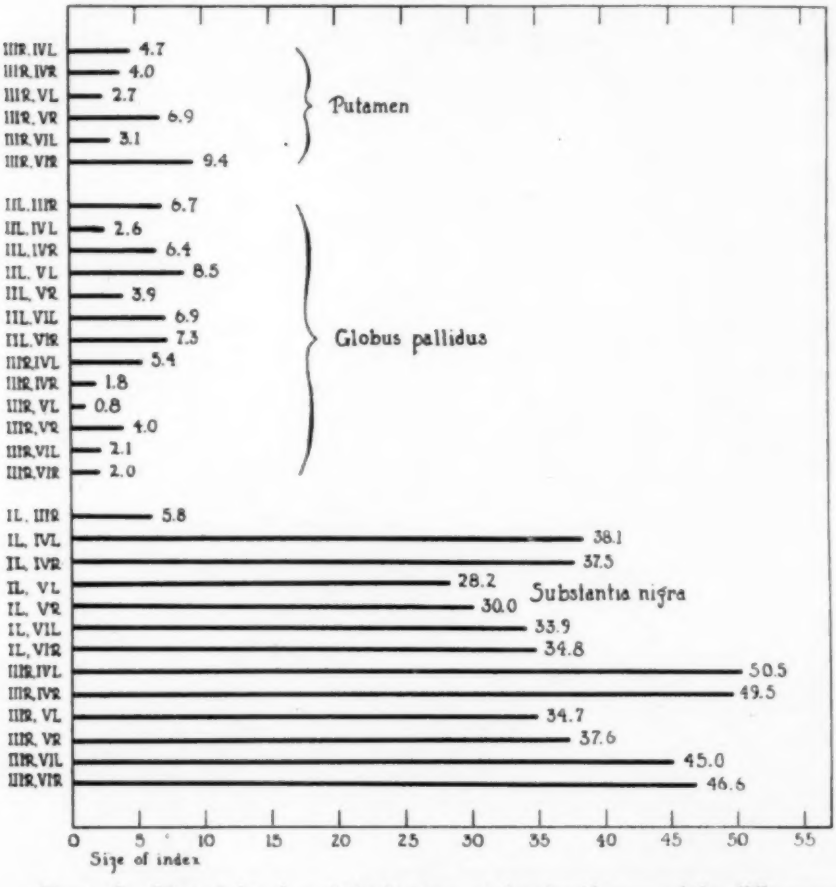


Chart 17.—Plot of the size of the indexes of the significance of the differences of the averages of the various counts in the parkinsonian cases compared with normal cases. The differences have about an equal significance in the putamen and globus pallidus, but in the substantia nigra they have a much more marked significance owing to the reduction in the number of cells.

disappeared, and the cells of the zona reticularis have become still less abundant. It is interesting to recall that death in Case 5 was suicidal, and thus occurred before the disease had run its course. This fact is in accord with the findings in the brain in that the highest substantia

nigra counts in the parkinsonian material were found in this case, and the frequency curve takes on the characteristics of the normal, at least in part.

Previous mention has been made of the paper of Lhermitte, Kraus and McAlpine.[10] They enumerated the cells in six "low power fields" of the globus pallidus and compared them with a like number from a normal case. From these observations they estimated a loss of 50 per cent. of the cells. Now six fields with a 10 × ocular and a 16 mm. objective (the conventional "low power") represent approximately 1.08 observations of ten square millimeters each. These six fields correspond so closely to one observation in the present study that, for purposes of comparison, they may be considered as one such observation. Glancing at the frequency distribution of the globus pallidus counts, it is conceivable that one observation might, in a normal case, range from 40 to 130 cells. It can then be seen that if only one observation is taken a count of 40 might be obtained for the suspected case and 130 for the normal (or vice versa), and from these findings a cell loss of 69 per cent. for the abnormal case be assumed, while in reality the two figures are merely the lower and upper limits of variability of the normal. The counts by these writers are of no significance.

SUMMARY AND CONCLUSIONS

In two additional cases of postencephalitic paralysis agitans studied by ordinary histologic methods, minimal changes of the globus pallidus but massive lesions of the substantia nigra were found. Scattered lesions found in other parts of the brains were so insignificant as to require no intensive investigation.

The two foregoing cases and a previously reported case have been studied by micrometric methods in order to evaluate quantitatively the amount of cell destruction in the lenticular region and substantia nigra.

Comparing with the normal cases, no decrease in the number of cells in the putamen or globus pallidus can be demonstrated.

An average decrease in the number of neurons of from 58 per cent. to 87 per cent. has occurred in the substantia nigra in the three cases.

From these data it appears that the syndrome of paralysis agitans may occur without a significant lesion in the globus pallidus, though this is not intended to mean that the globus pallidus never plays a rôle in parkinsonianism.

The destruction in the substantia nigra seems to be the essential factor in the production of the syndrome, at least in the three cases presented.

Micrometric methods are of great value to the neuropathologist and should be more commonly employed.

CEREBRAL SYMPTOMS INDUCED BY ANGIO-NEUROTIC EDEMA *

FOSTER KENNEDY, M.D., F.R.S.E.
Professor of Neurology, Cornell University Medical College
NEW YORK

Some of the phenomena to which I shall refer have been described before, but usually without emphasis, so that they have been forgotten. We are familiar with the appearance of "wet brain," but we do not think easily of circumscribed cerebral edema. Further, repetition has served for proof that brain vessels are incapable of variation in size, and this, despite the presence of a muscular coat in the walls of the cerebral arteries, the known ability of epinephrin to blanch the cortex as it does the skin, and my own observation [1] of sudden cortical devascularization as the first evidence of the onset of an epileptic seizure in a person not under the influence of a general anesthetic.

It is not easy to produce visible and palpable proof of angioneurotic edema affecting the brain, because no necropsy material exists on this subject, and were it obtainable, such circumscribed dropsies would be difficult to demonstrate. The traces of such evanescent processes would be apt to be obliterated by the act of death or by fixing fluids. However, it has been my fortune to observe many attacks of acute transient edema of the optic nerve and retina, to watch the onset, the passing and the structural effects of such events, and to observe, in the same patient, phenomena affecting other areas of the central nervous system—in the medulla, in the capsule, in the nerves of hearing, invisible to the eye but visible to the intelligence as being identical with those seen by the ophthalmoscope.

The disease associated with Quincke's name, according to Cassirer,[2] appears in two classes of persons or from two general causes: One kind comprises those proceeding from a toxic, autotoxic or infectious condition, with crises closely resembling anaphylactic attacks (febrile urticaria), with no tendency to recurrence, provided the cause be not repeated; to the other group belong all cases of hereditary or personal neuropathy in which the crises appear without relation to the intake of special foods or toxic exogenous factors. In these patients, in whom a vagotonic disposition is often demonstrable, the

---

* Read at the Forty-Eighth Annual Meeting of the American Neurological Association, held at Washington, May, 1925.

1. Kennedy, Foster: Epilepsy and the Convulsive State, Arch. Neurol. & Psychiat. **9**:567-575 (May) 1923.

2. Cassirer, R.: Die vasomotorisch-tropischen Neurosen, Monograph, Berlin, 1912.

cause of the disease is a purely nervous mechanism consisting of paralysis of the vasocontractors with escape of lymph.

This discrete classification is too diagrammatic to contain all the facts of this disease. It is common to find families all of whose members are subject to anaphylactic shock from invasion by special protein, and such persons must be included in both of Cassirer's groups. Nor is such classification accepted by others who have studied this question, as for instance by Bolten,[3] who believes that the disease is never an independent entity but is always a secondary condition based on sympathetic hypotonia due either to congenital functional inferiority or to neurotic processes in the central or peripheral portions of the sympathetic system through infectious toxemic factors. We are less concerned, however, at the moment with the morbid action underlying this disease—and it would seem as though many agents may produce these effects in suitable persons—than with the fact that this condition may give rise to highly dramatic events in the function of the central nervous system. Ullmann [4] reported the case of a man subject to transient swellings on the back of the hands, in the pharynx and laryngeal mucosa, which were followed by symptoms of cerebral pressure, syncope and focal epilepsy. This author thought that the complete subsidence of these grave cerebral symptoms in the course of a few days, the relatively rapid and entire recovery of the patient, and the later absence of convulsions after the disappearance of peripheral circumscribed dropsies made plausible the assumption of edematous changes in the brain and meninges. Oppenheim,[5] quoting this case, surmised that optic nerve disease might possibly develop on this basis, but recommended great caution in such an assumption; in Handwerk's [6] case and one of mine it was possible to show how accurate Oppenheim's hypothesis has proved to be. The same observer reported the combination of migraine, recurrent oculomotor paralysis and angioneurotic edema.

REPORT OF CASES

My first case was seen with Dr. Oscar Schloss. A physician's daughter, aged 2 years, otherwise healthy, had always been subject to attacks of giant urticaria. In June, 1923, six months before I saw her, she began to have attacks of screaming, in which she would clap her hands to her head which was thrown acutely backward. These attacks lasted about half an hour, and gave the impression of severe pain in the head; they took place three or four times a day, and on the day following these seizures, she had her most severe attack of urticaria on the arms, trunk and face. All these symptoms passed; two months later hives again appeared, on this occasion followed by attacks of

3. Bolten: Monatschr. f. Psychiat. u. Neurol. **45**:201, 1919.
4. Ullmann, K.: Arch. f. Schiffs u. Tropenhygiene **3**:176, 1899.
5. Oppenheim, H.: Textbook of Nervous Diseases, Ed. 7, Vol. 2, 1923.
6. Handwerk, C.: München. med. Wchnschr. **47**:2332, 1907.

screaming, and, after twelve hours, by generalized epileptic convulsions which lacked, however, any tonic phase, but which were clonic throughout, thus apparently being caused primarily by cortical irritation rather than by a sudden cutting out of the cortex and the transient production of a decerebrate rigidity such as characterizes the first phase of an ordinary epileptic seizure.[1] Eight convulsions, each of ten minutes' duration, occurred during twenty-four hours. Sedatives availed little. The spinal fluid was clear, normally constituted and under vastly increased pressure. The convulsions ceased after lumbar puncture, and for four months the child remained well. Urticaria then reappeared followed after a week by fits of screaming and then by nine convulsions apparently uninfluenced by morphin or chloral. Thirty cubic centimeters of spinal fluid were removed, again under immense pressure. The convulsions then ceased. Hypertonic saline was given intravenously. A month later circumscribed edema had appeared again, but yielded to belladonna, epinephrin residue and restriction of fluids. Protein sensitization tests proved her susceptible to milk. This food was discontinued, with the result that for seventeen months neither urticaria, headache nor convulsions have appeared. The child apparently has not suffered from the storms through which she has passed.

My second case was seen in consultation with Dr. Arthur Neergaard. An otherwise healthy middle-aged man for ten years had suffered from attacks of acute circumscribed edema affecting the soft palate, lips, cheek and occasionally the arms and trunk. Food tests had failed to reveal any especial susceptibility; kidney function, blood chemistry and blood pressure were normal. During the year preceding our consultation this patient had had no less than four attacks of hemiplegia, two affecting the left side and two the right, coincident with acute urticaria. Both episodes involving the left side of the brain were accompanied by complete motor aphasia, and in no instance was there any sign of disease to be found thirty-six hours after its inception.

My last, most severe and most important case was referred to me by Dr. Biram of Hartford, Conn., in October, 1923. A man, aged 28, for five years the subject of swellings varying in size from that of a pea to that of a walnut, occasionally becoming superficial but usually deeply seated in the muscles, was admitted for observation to the Neurological Institute. If such a swelling occurred near a joint, such as the wrist, for the duration of the swelling—from two to six days—the joint was disabled through stiffness and pain. These swellings occurred suddenly; within an hour, they were tender, painful and throbbing, and, when the skin was involved, itchy. They occurred in the arms and legs and occasionally in and on the trunk muscles. Professor Fordyce diagnosed this condition acute circumscribed edema. Two years after their inception, and during the course of an attack, he began to be sleepy, to experience a dull headache and to notice suddenly that lights seemed foggy or prismatic; in a few hours he discovered that he could no longer see with the right eye, the ball of which was acutely tender and surrounded by an area of pain. In about six weeks vision returned to normal.

A year later vision was lost totally in the left eye, and completely recovered in a fortnight. The other phenomena were identical with the previous episode. Ten months later, the right eye was attacked and recovered. I saw him on October 15, when left vision, having disappeared two weeks before, had returned, so that he could count fingers with the affected eye at a distance of 4 feet. Between his attacks of blindness he was well, except for occasional

swellings in the muscles and skin. The blood chemistry, Wassermann test, renal function, calcium content and basal metabolism were normal. The blood pressure never rose above 110. The left pupil was irregular in shape, sluggish to light and on convergence; the left fundus could be seen but hazily by reason of vitreous opacity. In a few days the reaction of the pupil became as brisk as that of its fellow; the fundus was seen clearly, and vision was fully restored. He left the hospital at the end of October in perfect health. A week later he had another attack of deep swellings in both forearms, then came a stabbing pain in the forehead, so that he screamed continuously for some hours, during which he began to lose vision in both eyes; he became stuporous, and a left hemiplegia appeared. Three days later the stupor had passed, but he had no perception of light in either eye; the pupils were irregular and fixed, and no fundal light reflex could be obtained. He only partly recovered from the left hemiplegia in the course of the next four months.

The vitreous body began to clear up in a week, and one began to get fleeting glimpses of the fundal vessels as though through puffs of smoke which rose or moved from side to side in front of the disk, a moving, partly translucent, partly transparent cloud which was clearly being thrown into the vitreous; the nerve heads seemed blurred in outline, but by the time the smokiness of the media had disappeared, the papillae again looked clear cut. Paracentral scotoma could be seen for two days, after which both fields and vision were again normal.

On Dec. 19, 1923, swellings again appeared in the substance of the anterior tibial muscles; the next day speech seemed to be somewhat thick; two days later, more swellings appeared; the patient was drowsy and had pain over the right eye, with decreasing monocular vision. The right pupil began to react sluggishly to light, and the appearance of puffs of smoke or mist was again seen with the ophthalmoscope, increasing in density until the right fundus passed out of sight, when vision also disappeared. On this day a large, red, boggy swelling appeared around the third metacarpophalangeal joint of the left hand. Two days later there was complete aphonia, and the patient was deaf in both ears. He could not hear the tuning fork on contact. There was much difficulty in swallowing, as the palate was paralyzed, and he could not move the tongue into the left cheek. The blood pressure dropped to 90 systolic. Respiration was labored. The mind remained clear. While vision improved in the right eye, it deteriorated in the left, and vitreous opacities appeared on that side as they began to clear on the other. Speech was absent, and alternating incontinence of urine and feces appeared.

On January 17 definite signs of improvement were seen; swallowing was less difficult; slight movement of the palate returned; vision was restored; sphincter control was reasserted. Deafness was still absolute, although Dr. Sowers could find no defect in the ear drums. Ten days later he could talk intelligently, although with bulbar inflection; he could sit up, and he could hear loud conversation with the left ear. On January 30 he could hear a watch on contact with each ear, and on February 7 hearing was restored to normal. Through all these extraordinary fluctuations of function, only moderate improvement occurred in the left hemiplegia, which behaved in its course as such affections of thrombotic origin usually do. Lumbar puncture was not performed on this patient on account of the risk. Dr. Cook found equivocal sensitization reactions to milk and veal, but the patient had had asthma in childhood, and his mother always had urticaria after eating fish.

COMMENT

These cases are dramatic and rare. Acute perivascular edema may play a part in some of the malignant types of insular sclerosis. If external poisons can cause cerebral episodes such as those I have described, they may also cause the transient episodes of Charcot's disease, of which the morbid process has been so baffling and the therapy so mystical and inane.

DISCUSSION

Dr. Edward A. Strecker, Philadelphia: I was fortunate enough to see Dr. Kennedy's case in Philadelphia about six months subsequent to the study at the Neurologic Institute. The patient was stone deaf and practically blind. There was still the residual left hemiplegia. The spinal fluid examination was negative.

Dr. Hermon C. Gordinier, Troy, N. Y.: I would like to narrate a case which perhaps belongs to the group which was just described. The patient, whose age was 28, was suddenly seized with a convulsion, Jacksonian in type, followed by coma, right sided hemiplegia and apparently total aphasia.

On the following morning he had recovered consciousness, but he still had a hemiparesis of the whole right side and very definite motor aphasia. In the course of about a week or ten days, the symptoms had disappeared and he was perfectly well. There was a distinct history of previous attacks of spasmodic asthma in this case.

Dr. Adolf Meyer, Baltimore: In view of the serious effects that an acute disturbance of that sort can have, I ask whether in such cases salt solution has been systematically tried, inasmuch as it might at least help in avoiding undue blocking and undue risks of thrombosis produced by temporary local compressions.

Dr. Peter Bassoe, Chicago: A man whom I saw in 1910 presented the picture of increased intracranial pressure, headache, choked disk and vomiting, without localizing symptoms and without history of any other disturbances. He had a decompressive operation, improved gradually and went out to the Pacific coast.

He turned up in Chicago about fifteen years after the decompressive operation, in another hospital, under the observation of very competent men for severe angioneurotic edema, with swellings of large areas of the body, and, I believe, some intermittent hydrops of the joints.

The question arises as to whether the early picture of increased intracranial pressure might not have been produced by angioneurotic edema of the brain, which was the first indication of the condition.

Dr. Bernard Sachs, New York: The splendid value of Dr. Kennedy's contribution would be somewhat lessened if we were to apply the statements he made only to angioneurotic edema, which is perhaps one of the rarest of all diseases we are apt to come in contact with; but the lesson I have drawn from his contribution is that we are all very apt to under-rate the general effect of cerebral edema in a number of different conditions, such as cerebral hemorrhage and even in the cases of encephalitis.

Dr. Foster Kennedy: In closing: I am very much interested in hearing the subsequent report of my third patient. He had recovered, on February 7, functions of hearing and swallowing, and so forth, though he still had bulbar speech; so that after I saw him, he must have had another episode which produced permanent effects.

I am very much obliged to Dr. Sachs for following up my thought, that these edemata, particularized in Quincke's disease, may occur in a great many conditions. I believe many of the transient episodes of encephalitis must be edematous in mechanism, and many of the transient hemiplegias which we see in middle life, can hardly be based on a transient thrombosis, particularly the phenomena which we see in acute multiple sclerosis may very well be dependent on an acute, local edema of the brain, around a blood vessel.

My thought about the hemiplegia which persisted may have seemed a little confused. It behaved exactly as thrombotic hemiplegias are apt to behave, so it may have been that a thrombosis occurred in the course of a very severe, one-sided cerebral edematous outpouring, or it may be that the edema was so great as to produce permanent structural damage. That may have occurred by now in the auditory nerves, and it would not be surprising if the fluid output was sufficient for the fibers into which the fluid was poured to suffer permanent destruction. I rather think that the machinery of insular sclerosis is that fluid is poured out from a vessel, around the vessel, and produces severe functional disturbances through physiologic block, absorption of fluid later takes place, and only a small residuum of anatomic block persists.

Dr. Meyer mentioned hypertonic saline. That was used in one of the cases and seemed to be of value, and it was used in a third case and seemed to be of no value. I did not go into all the therapeutics which we adopted in the case which we observed for so many months, as it would have made my paper unconscionably long, but it was very clear that all we did was of no avail.

TRICHINOSIS ENCEPHALITIS

A PATHOLOGIC STUDY *

GEORGE B. HASSIN, M.D.
Associate Professor of Neurology, College of Medicine, University of Illinois; Histologist to Illinois State Psychopathic Institute
AND
ISADORE B. DIAMOND, M.D.
Assistant Professor of Neurology, College of Medicine, University of Illinois
CHICAGO

Notwithstanding the exceedingly rich literature on trichinosis, few contributions treat of the neurologic or neuropathologic phase of this infection, and practically none deals with the changes that result from the presence of *Trichinae* in the brain tissues. Only Frothingham,[1] who succeeded in demonstrating these worms in the brain, gives a superficial description of the concomitant changes. These were rather meager—"slight hemorrhages without cellular reaction and areas of cellular infiltrations consisting chiefly of endothelial and neuroglia cells with an occasional leukocyte and lymphocyte. In such an area part of a trichina embryo sometimes appears outside the vessels."

The case here recorded is thus the second in the literature in which the invasion of the brain by *Trichina* larvae has been demonstrated together with its effect on the central nervous system.

REPORT OF A CASE

History.—A boy, aged 14, admitted Nov. 30, 1924, to the medical service (Dr. Weatherson) of Cook County Hospital, two weeks before admission became ill with general malaise, diarrhea, stiffness and pain in the extremities. His mother and a sister, aged 19½ years, were also under observation in the hospital for a similar condition.

Examination.—The patient was toxic, "semidelirious" and perspired profusely. His temperature was 102 F., pulse rate 120 and respiration 28. The eyes were inflamed, the lips dry and covered with sordes. The muscles, especially those of the legs, were tender but not paralyzed. Signs of meningitis and of cranial nerve involvement were absent. The heart, lungs and abdominal organs were normal. An excised piece of muscular tissue (from the gastrocnemius) revealed numerous *Trichinae,* few of which were encapsulated.

---

* From the pathologic laboratories of the Research and Educational Hospitals of the University of Illinois and the State Psychopathic Institute.

* Presented by title at the Fifty-First Annual Meeting of the American Neurological Association, Washington, D. C., May 5, 1925.

1. Frothingham, Channing: A Contribution to the Knowledge of the Lesions Caused by Trichina Spiralis in Man, J. M. Res. **15**:483, 1906.

The blood examination revealed 25,200 white cells, of which 70 per cent. were polymorphonuclears, 21 per cent. eosinophils, 1 per cent. basophils, 6 per cent. lymphocytes and 2 per cent. monocytes. The urine was normal; the spinal fluid was not examined.

Course.—Most of the time the patient was restless, sometimes irrational, occasionally noisy or stuporous and drowsy. Muscular twitchings in the feet were frequent. Diarrhea was persistent, the stools being liquid, brown, offensive. The temperature was as high as 105 F., with a pulse rate of 144 and a respiration rate of 38.

Treatment consisted of intravenous injections of 1 per cent. solution of antimony and potassium tartrate. Death occurred, Dec. 4, 1924, twenty-two days after the onset of the illness.

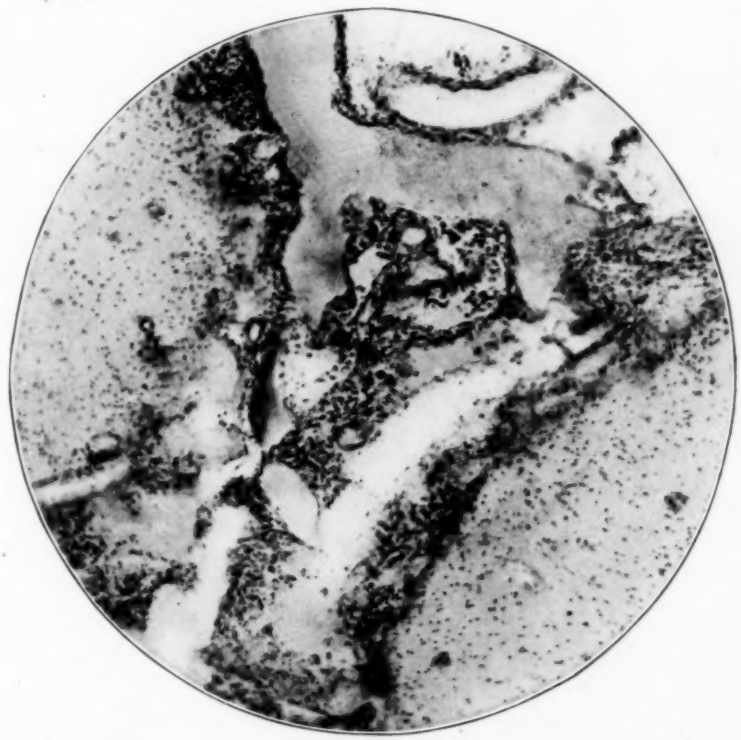


Fig. 1.—Infiltration of the cerebral pia-arachnoid. Toluidin blue stain; × 65.

Gross Necropsy Findings (Dr. Rappaport).—The findings were: Generalized (acute) muscular trichinosis, increased cerebrospinal fluid, acute hyperplasia of the spleen, lymphoid hyperplasia of the intestinal mucosa, acute interstitial myocarditis, moderate dilatation of the right ventricle, fatty changes and passive hyperemia of the liver, moderate edema of the lungs, sordes of the lips and a surgical wound of the calf of the left leg.

The pia of the brain was transparent and in some areas markedly congested; the sulci, especially in the frontal lobe, were gaping; the gyri were of normal size and not flattened. The base of the brain showed no abnormalities; the ventricles were not dilated, and the cortical gray matter was sharply defined

from the white substance. The cerebral parenchyma was congested, without foci of softening or hemorrhage. The spinal fluid removed at the necropsy showed numerous trichina larvae (verbal report by Dr. Rappaport).

Microscopic Examination.—The pia-arachnoid, throughout the cortex and the base of the brain, was markedly infiltrated (Fig. 1), some areas (occipital and Ammon's horn) more, some (frontal lobe, cerebellum) less. The infiltrative elements in some regions (cerebellum), were mostly large lymphocytes in the form of homogeneous, pale, round or slightly oval bodies containing an eccentric nucleus fairly rich in chromatin. In other areas mesothelial cells predominated and often formed clusters. As a rule, these types of cells were mixed with a

Fig. 2.—Pia. In the center of the picture is a *Trichina* embryo surrounded by cell elements described in text. Toluidin blue stain; × 800.

great variety of other elements—plasma cells, fat granule bodies (gitter cells), fibroblasts and macrophages, which sometimes contained within their vacuoles lymphocytes or polymorphonuclear leukocytes. The latter were mostly eosinophils freely mixed with the foregoing cell bodies. These occasionally formed dense masses or foci, near or within which were sometimes present round, slightly curved bodies filled with a large number of intensely stained granules (Fig. 2). Morphologically, these granular structures resembled typical embryos of *Trichina*. They were absent in the blood vessels, which were slightly infiltrated and markedly congested. Hemorrhages and blood pigment granules were absent, but red cells, mostly well preserved, were abundantly scattered among the cellular elements

described. In general, the pia-arachnoid changes may be designated as an acute nonsuppurative leptomeningitis.

Some areas in the frontal lobe of the brain and in the pons exhibited numerous small, round or oblong cavities (Fig. 3). These were for the most part empty; some contained a collapsed blood vessel, the walls of which were sometimes connected with the surrounding parenchyma by strands of glia tissue. In rare instances, the cavities were adjacent to or surrounded ganglion cells, while the brain substance itself appeared slightly rarefied. Such areas of rarefication harboring cavities were in sharp contrast to the contiguous regions densely filled with dendrites, glia cells and blood vessels. However, in these apparently

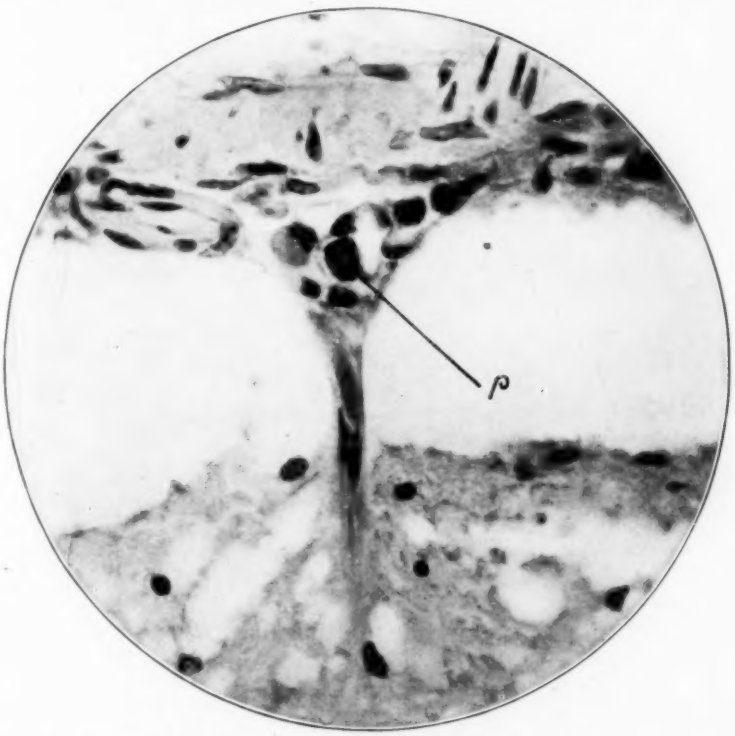


Fig. 3.—Pons. Lower third shows état criblé. The upper third contains an infiltrated adventitial space. At *P*, there is a plasma cell with two nuclei. Stain same as in Figure 1; × 560.

normal areas the glia was rarefied showing as so-called glia reticulum. Principally located in the pons and some portions of the frontal lobe, the cavities gave the sections a cribriform appearance described as état criblé. Most observers, following Nissl, consider this condition an artefact, some (C. and O. Vogt, and others) a pathologic condition, the result of disintegration of the brain tissue. Disintegration was quite evident in the basal portions of the pons, where so-called lacunae were present. These were large irregular cavities containing small remnants of detached brain tissue, a large number of hyperemic and infiltrated blood vessels, scattered red blood cells intermingled with polyblasts, many eosinophils

and macrophages packed with lymphocytes and polymorphonuclear cells. In addition, there were small islands or nodules consisting of glia cells and enclosing portions of *Trichinae* embryos, while the adjacent nerve tissue was rarefied, showing as glia reticulum.

The foregoing cell conglomerations or nodules were also present in brain areas that showed no disintegration. They appeared as granulomas (Fig. 4) and were cellular. The cells were exclusively glia elements rich in cytoplasm, the nuclei of which were polygonal and exceedingly polymorphous; that is to say, they greatly varied in shape and size. The majority of the cytoplasmic cells through their processes were fused or blended, forming a syncitium. The nodules invariably harbored a *Trichina* embryo, whole (Fig. 5) or a fragment of it,

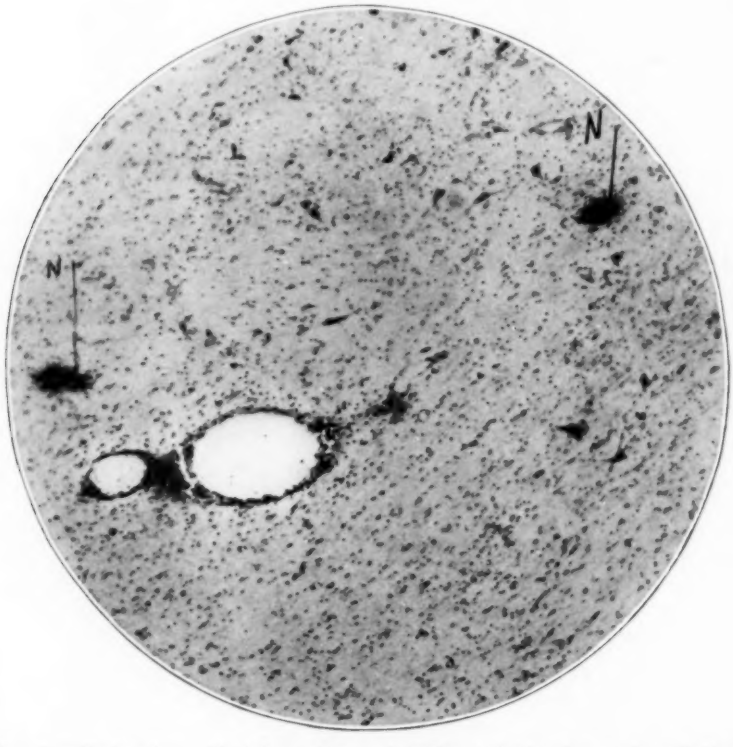


Fig. 4..—Peduncles. Nodules (*N*) and infiltrated blood vessels. Stain same as in Figure 1; × 60.

but no blood vessels or ganglion cells. They were scattered in large numbers throughout the white brain substance, basal ganglia, pons and cerebellum, but were absent in the cortex. The spinal cord was not removed.

In rare instances a stray *Trichina* (Fig. 6) was encountered in the parenchyma. As Figure 6 shows, the worm appeared unusually large and thick, containing an enormous amount of brightly stained granules. These filled the entire body, except a small, somewhat narrower portion at one of the poles, where the granules were rather sparse (the mouth of the *Trichina* embryo). Reactive glia or vascular phenomena were lacking in contrast to what was seen in the nodules, but

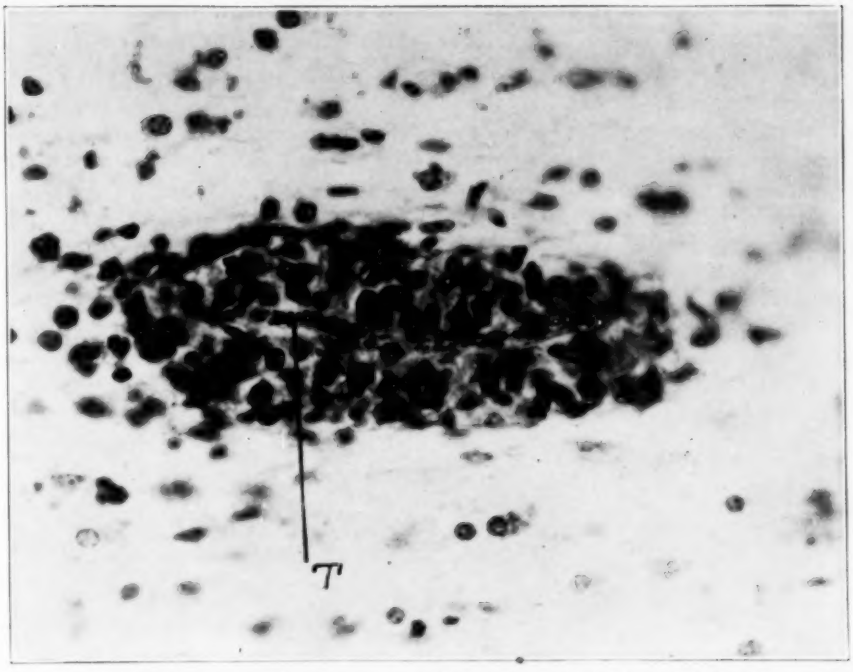


Fig. 5.—Higher magnification of a nodule with a *Trichina* (*T*) in the center. Stain same as in Figure 1; × 560.

Fig. 6.—*Trichina* in the nucleus caudatus. The ganglion cell to the right shows neuronophagic phenomena. Stain same as in Figure 1; × 700.

the neighboring ganglion cells (Fig. 6) showed marked satellitosis and neuronophagia.

There were equally pronounced changes in the blood vessels. Throughout the cortex, midbrain, medulla and other regions the arteries as well as the veins were greatly infiltrated (Fig. 7). The infiltrative cells were for the most part large lymphocytes or polyblasts, often mixed with eosinophils, plasma cells and fibroblasts. The blood vessels were also densely hyperemic, and their endothelial as well as adventitial cells markedly hypertrophied and hyperplastic.

Dense as the perivascular infiltrations were, they were strictly confined within the limits of the adventitial spaces of Virchow-Robin, never invading the surrounding parenchyma. In some instances, the infiltrations were so dense (Fig. 7)

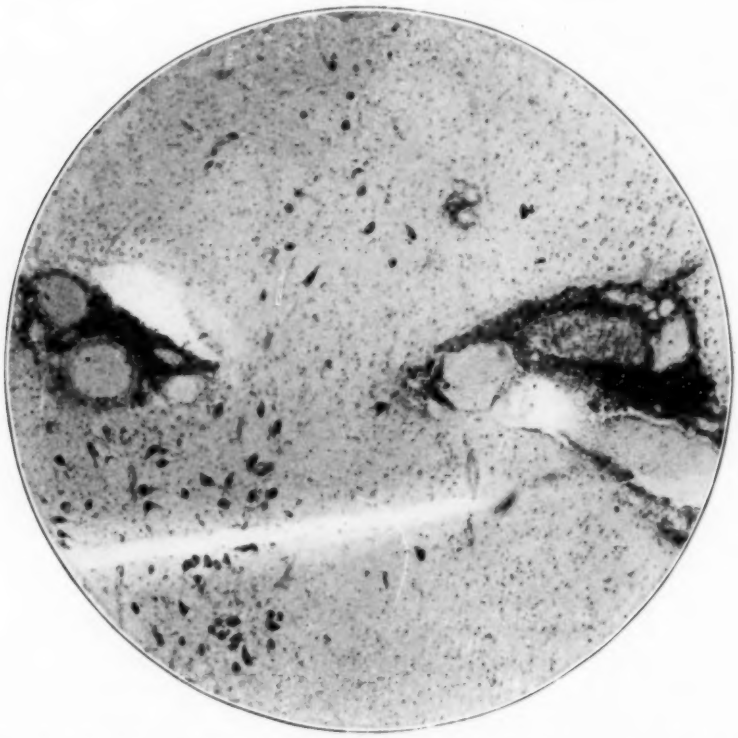


Fig. 7.—Conglomerations of intensely infiltrated blood vessels. The infiltrations reproduced under higher power in Figure 8. Stain same as in Figure 1; × 60.

that at the first glance, under a lower power lens, they somewhat resembled the nodules described above. Morphologically, however, they differed, for they consisted, not of ectodermal, but of mesodermal, hematogenous, elements. But like the nodules, they harbored *Trichinae* embryos (Fig. 8), which were not found within the blood vessels. Hemorrhages, in the form of small foci, occasionally were present around a capillary or small blood vessel, but they were most likely agonal, as reactive phenomena on the part of the glia were lacking.

In contrast to the larger blood vessels, the capillaries exhibited no signs of adventitial infiltration, but their endothelial layer was markedly hypertrophied,

was stained densely and had a garland-like appearance. Stained with scarlet red, the capillaries as well as the arteries and veins uniformly showed the presence of lipoid substances in the form of granules or large drops.

The ganglion and glia cells were markedly changed. The former showed various stages of degeneration, from a more or less pronounced chromatolysis to cell sclerosis or a complete destruction of the cell body—its breaking up and invasion by neuronophages (Fig. 9). In scarlet red specimens they were more or less filled with lipoids. Though diffuse, such degenerative changes were especially in evidence near the nodules and very slight in the cerebellum. The ganglion cell changes, regressive in character, were associated with progressive or proliferative phenomena in the glia. Thus, in some areas, especially around the

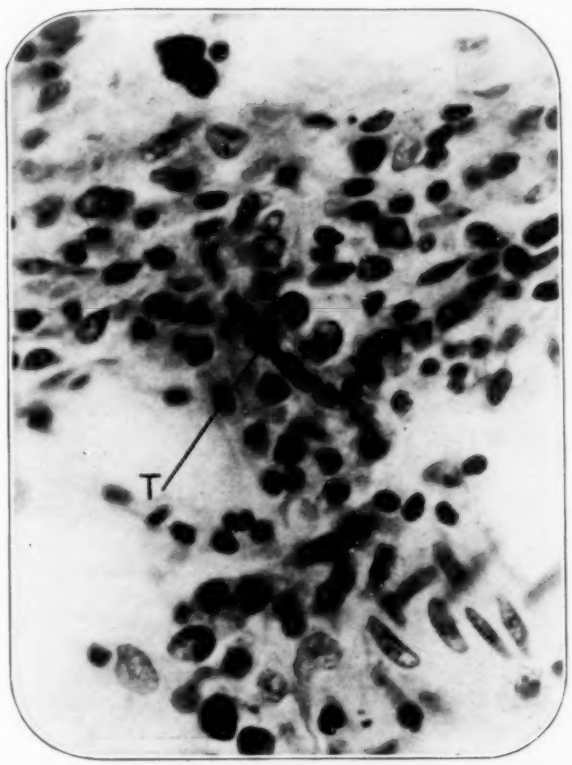


Fig. 8.—Focus of infiltration enclosing a *Trichina* (*T*). Stain same as in Figure 1; × 700.

Sylvian aqueduct, the visual field appeared densely covered with glia nuclei. As a rule, the glia cells were rich in cytoplasm and formed syncitia which like the nodules and adventitial infiltrations contained *Trichina* embryos (Fig. 10).

No changes were evident in the tuft cells of the choroid plexus, but the blood vessels were congested, not infiltrated, and the stroma appeared exceedingly cellular and hyperplastic. In the spaces outside the tufts or choroid villi, that is to say lying freely in the cavity of the fourth and lateral ventricles, were present *Trichina* larvae (Fig. 11) resembling in their general appearance those found in the parenchyma of the brain tissues.

SUMMARY AND COMMENT

The histologic changes may be defined as diffuse, degenerative and inflammatory,with marked hyperplastic phenomena in the pia-arachnoid, choroid plexus and glia (syncitia and nodule formation). Typical of acute encephalitis, they were associated with the presence of *Trichina* embryos in the cerebral parenchyma, nodules, infiltrated adventitial and subarachnoid spaces and in the cerebral ventricles.

The changes outlined strikingly resemble those of other types of

Fig. 9.—Marked neuronophagia. The basal dendrites are markedly swollen. Stain same as in Figure 1; × 300.

acute nonsuppurative encephalitis, such as those seen in Heine-Medin's disease, and especially in typhus fever.[2] But while in the latter variety the nodules are said to be especially abundant in the medulla, in this case they were rather evenly distributed throughout the brain, affecting the

2. Hassin, G. B.: Brain Changes in Typhus Fever Contrasted with Those in Epidemic Encephalitis and Acute Poliomyelitis, Arch. Neurol. & Psychiat. **11**:121 (Feb.) 1924.

medulla probably less than other portions. In typhus fever the perivascular infiltrations, mainly in the form of plasma cells, are preferably around the small blood vessels and capillaries, while in this case they were mostly of large lymphocytes around the larger blood vessels. A bush-like glia proliferation, roset and stellate formations so frequent in typhus fever were absent here, although glia syncitia were common.

We thus find here some difference in reactive phenomena on the part of both the glia and hematogenous elements, which is evidently

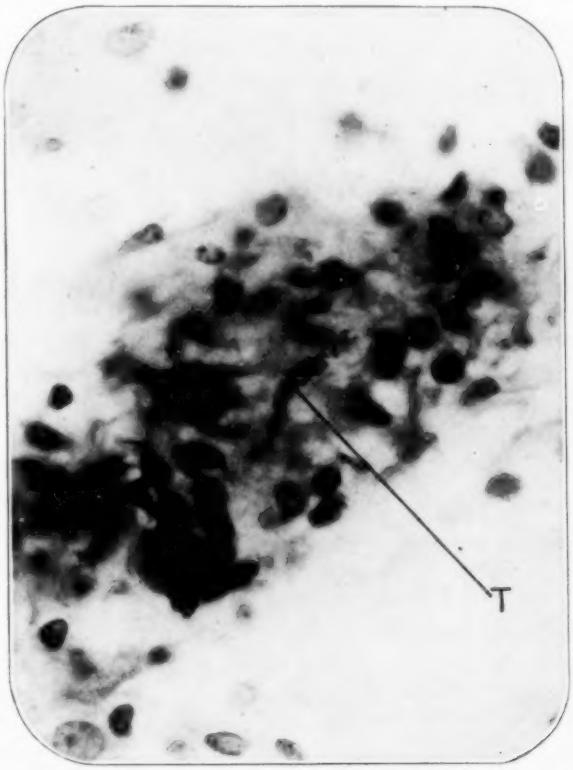


Fig. 10.—Optic thalamus. Glia syncitium containing a *Trichina* (*T*) embryo; × 800.

due to the difference in the virus. The oustanding features in this case —the nodules and perivascular infiltrations—are therefore to be considered as manifestations of a reaction against the infection. This was in the form of *Trichina* embryos which were thus responsible for the excessive cellular proliferations in the nodules and around the blood vessels. The inference is that in other types of encephalitis the exact etiology of which has not yet been established, the presence of nodules

and perivascular infiltrations denotes an infection.[3] In such forms of encephalitis (epidemic encephalitis, typhus fever, Heine-Medin's disease), the morbid agent is most likely hidden in the nodules and the perivascular infiltrations but so far has not been detected, probably because of deficient technic.

Besides the infiltrations, nodules and syncitia—purely local reactive phenomena—a much more important finding deserves consideration; namely, the diffuse degeneration with accumulation of lipoids. This is a manifestation of intoxication caused by *Trichinae* in the brain tissues. Flury [4] not only succeeded in isolating toxins from the muscles invaded

Fig. 11.—Fourth ventricle. In the center of the picture a typical *Trichina* embryo. Hematoxylin eosin stain; × 700.

by *Trichinae*, but by injecting them into animals he produced all the symptoms and signs of trichinosis "without the active participation of living trichinae." Furthermore, Flury demonstrated that toxins do originate also from the affected, decomposed, muscular tissue and that through the combined action of the muscle toxins and the catabolic products produced by the parasite, a double toxic injury occurs.

3. Hassin, G. B.: The Contrast Between the Brain Lesions Produced by Lead and Other Inorganic Poisons and Those Caused by Epidemic Encephalitis, Arch. Neurol. & Psychiat. **6**:268 (Sept.) 1921.

4. Flury, F.: Beiträge zur Chemie u. Toxicologie der Trichinen, Arch. f. Exper. Pathol. u. Pharmacol. **73**:164, 1913.

Flury's remarkable findings were corroborated by Gruber,[5] and there seems to be no doubt that in trichinosis the marked toxic condition is due to the absorption of both the endogenous (caused by the *Trichinae*) and the exogenous (caused by the decomposed muscles) products. The resulting toxemia is on the whole much more dangerous than the various inflammatory phenomena described, for the latter may disappear, become absorbed and result in recovery. The degenerative phenomena, in contrast, cause irreparable damage and death. In fact, the degenerative conditions may be the sole clinical and pathologic manifestation of trichinosis, as in a case reported by Bloch and one of us.[6] A patient, aged 23, showed marked toxic phenomena, with a high temperature, delirium and convulsions. Spinal puncture yielded no *Trichinae*. They were found in the stool in large numbers. Microscopic examination showed no *Trichinae* in the brain, no infiltrations, nodules or syncitia, but there was a marked état criblé, glia reticulum and neuronophagic phenomena, with other signs of severe ganglion cell lesions, but without accumulation of lipoids. This case seems to corroborate Flury's experimental observations that in trichinosis a clinical picture of toxemia may obtain solely from the presence of toxic products. The pathologic findings in such cases necessarily differ from those in which we deal with an additional factor—the presence of *Trichinae* themselves.

It is rather strange that even the best and most exhaustive treatises on trichinosis, such as Stäubli's,[7] do not even mention the possibility of brain invasion by this parasite. Yet the presence of *Trichina* embryos in the cerebrospinal fluid described by Van Cott and Lintz,[8] Bloch,[9] Elliot,[10] Cummins and Carson,[11] Salzer,[12] Meyer [13] and Prym,[14] indicates that the central nervous system may be invaded. Salzer's statement is

5. Gruber, G. B.: Neue Studien ü. die Pathologie der Trichinen, München. med. Wchnschr. **61**:645 (March 24) 1914.

6. Bloch, L., and Hassin, G. B.: Trichinosis complicated by encephalitis, M. Rec. **91**:537 (March 31) 1917.

7. Stäubli, C.: Trichinosis, Wiesbaden, J. F. Bergman, 1907.

8. Von Cott, J. M., and Lintz, W.: Trichinosis, J. A. M. A. **62**:680 (Feb. 28) 1914. Lintz, W.: Trichinosis and C.-Spinal Fluid, ibid. **62**:1856 (June 10) 1914.

9. Bloch, L.: Trichinosis. Report of a Case with the Trichinae Larvae in the Spinal Fluid, J. A. M. A. **65**:2140 (Dec. 18) 1915.

10. Elliot, A. R.: Trichinosis. Report of a Case with Trichinae Larvae in the Spinal Fluid, J. A. M. A. **66**:504 (Feb. 12) 1916.

11. Cummins, W. T., and Carson, G. R.: A Case of Trichinosis with Embryo in the Spinal Fluid, ibid. **66**:1856 (June 10) 1916; **67**:806 (Sept. 9) 1916.

12. Salzer, B. F.: A Study of an Epidemic of Fourteen Cases of Trichinosis with Cures by Serum Therapy, J. A. M. A. **67**:579 (Aug. 19) 1916.

13. Meyer, J.: Trichinosis, J. A. M. A. **70**:588 (March 2) 1918.

14. Prym, P.: Ueber Trichinose beim Menschen, Centrabl. f. allg. Path. u. Bacteriol. **34**:89, 1923.

significant. He asserts that *Trichinae* were readily found in the cerebrospinal fluid in eight of fourteen cases; in one case, a child of 3 years, three months after clinical recovery. He also states that "trichinae occurred abundantly in the brain." On injection of such tissue into animals Salzer could produce the disease. Salzer's report, which was preliminary, without photomicrographs and without description of histopathologic changes, is, naturally, less valuable than that of Frothingham.[1] In our case, *Trichinae* were abundant, and their presence in the brain is of great scientific value, for it definitely settles the much discussed question as to how they travel from the intestines to various tissues, especially the muscles. Leuckart explained the transportation of *Trichinae* to the muscles by their active migration. He believed that *Trichinae* embryos born in the lumen of the intestines pierce the walls and enter the peritoneal cavity. From here they travel along the tissue spaces to their goal, the striated muscles. Askanazy,[15] Romanovich [16] and Graham [17] maintain that the transportation is not an active but a passive process. Askanazy showed that *Trichinae* are born, not in the lumen of the intestines, but in their mucous membrane, where they are deposited by the females. Thence the embryos pass into the lymphatics and are carried to the thoracic duct, heart, blood vessels and the capillaries of the muscles. Breaking through the capillaries of the latter, they land in the muscle fibers, where they become encapsulated. Through successful demonstration by Graham of the presence of *Trichina* embryos in small arteries and by Stäubli in the blood, the migration of *Trichinae* is considered to be settled in favor of the "passive" theory. Our case affords additional proof of its correctness. *Trichina* embryos certainly could not cover the long distance from the intestinal canal to the brain by active, voluntary movements through the tissue spaces. It is more reasonable to assume that they were carried there by the blood stream, just as any other substance (e. g., carcinoma cells) is carried to the brain from remote organs by the lymph and blood channels. Reaching the cerebral capillaries, *Trichinae* provoke in them reactive phenomena—swelling of the endothelial and adventitial cells. Then they pierce the walls and land in the brain tissues, where they produce the nodules, syncitia and perivascular infiltrations. By the nodules and syncitia some of the embryos are kept from further propa-

15. Askanazy, M.: Zur Lehre von der Trichinosis, Virchow's Arch. f. path. Anat. **141**:42, 1895.

16. Romanovich: Recherches sur la Trichinose, Ann. de l'inst. Pasteur **26**:351, 1912.

17. Graham, J.: Beiträge z. Naturgeschichte d. Trichina Spiralis, Arch. f. mikr. Anat. **50**:219, 1897.

gation, being as it were destroyed on the spot, while others, like any other waste, are carried to the perivascular channels and from these to the subarachnoid space and the ventricles.

CONCLUSIONS

Trichinosis may produce a typical picture of acute nonsuppurative meningo-encephalitis.

It produces marked degenerative and inflammatory reactive phenomena.

The former are due to the toxins, the latter to the presence of *Trichinae*.

The *Trichinae* are harbored within large accumulations of cell elements—nodules, syncitia and perivascular infiltrations.

The invasion of the brain by *Trichinae* occurs through the lymph and blood vessels.

The elimination of *Trichinae* occurs by way of the adventitial channels into the subarachnoid space and the cerebral ventricles.

DIFFERENTIAL DIAGNOSIS BETWEEN CEREBRAL DEGENERATION, INFILTRATING CEREBRAL NEOPLASM AND INFILTRATING CEREBRAL NEOPLASM WITH DEGENERATION *

HENRY ALSOP RILEY, M.D.
AND
CHARLES A. ELSBERG, M.D.
NEW YORK

While the symptoms of cerebral hemorrhage and of cerebral embolism are well understood, the differentiation between a more or less slowly progressive degeneration of the brain secondary to thrombosis of larger or smaller cerebral arteries and some forms of infiltrating tumors is not so clearly defined, and the differential diagnosis between these two pathologic states and cerebral degeneration due to an infiltrating new-growth which has involved a large brain artery is often difficult.

When this study was undertaken, it was planned to consider the diagnosis between cerebral degeneration from thrombosis, and cerebral neoplasm, and we studied the records of our cases in which gross cortical softening and other degenerative changes had been found at the operating table. We then discovered a number of records of patients in whom a degenerated cortex had been exposed and a diagnosis of a vascular lesion had been made at the time of the operation. Some of these patients succumbed after weeks or months, during which the clinical symptoms either remained unaltered or new signs of disturbed function appeared, so that a tumor with degeneration was suspected before death. In the former, the postmortem examination usually showed that the degeneration seen at the operation was secondary to a deep infiltrating tumor, while in the latter, the diagnosis of tumor with degeneration was verified at necropsy.

The number of verified cases of cerebral degeneration from vascular disease was therefore materially reduced, and it was clear that from the evidence obtained at the operating table a diagnosis of primary cortical degeneration should be accepted with great reservation, for a tumor is often the cause of the vascular changes.

The following remarks are based on one case of cerebral degeneration proved at the necropsy table, one patient observed at operation and still

---

* Read by title at the Fiftieth Annual Meeting of the American Neurological Association, Philadelphia, June, 1924.

alive and in good health after nine years, four cases of extensive degeneration due to infiltrating tumors and a large number of cases of infiltrating tumor of the cerebral hemispheres.

CEREBRAL VASCULAR DEGENERATION

The anastomotic connections of the cerebral vessels are far less rich and extensive than those of the systemic and visceral blood vessels. In the final subdivisions, the cerebral vessels become terminal arteries and connect with no other channels, thus completely preventing the possibility of blood from other sources reaching the affected area except by reestablishment of the permeability of the occluded artery. The degree of tissue destruction which may follow closure of the lumen of a vessel depends on the completeness and duration of the nutritive interruption, but the many good recoveries that take place after apparently profound circulatory disturbances demonstrate that the recuperative powers of the brain tissue are great.

Diminution of the arterial circulation results in anemia with stagnation and venous congestion over the surface and about the borders of the region involved. Secondary changes soon ensue: myelin fragments and punctate hemorrhages appear; edema occurs; foreign cellular elements, both mesodermal and ectodermal, appear; the detritus is removed, and the process finally results in mesodermogenous and ectodermogenous scar tissue. The first macroscopic change is due to anemia and is the so-called "stage of white softening." As the process continues, the congestion and extravasation transform the originally pallid area into a suffused hemorrhagic one—the "stage of red softening"—which gradually, by the reduction of the liberated blood pigments and the transformation of the myelin into simple fats, results in the "stage of yellow softening." The removal of this material results in the production of a depressed area covered by edematous leptomeninges, the area finally healing by the action of the connective tissue and glial elements. The most important factor in the removal of the yellow material is the fat granular cell, the so-called gitter cell, which may be found in such enormous numbers as almost to form a tissue of its own. Ingrowths from the pia occur over the immediate site of damage, with calcification or cystic formation. These cysts consist of a neuroglial wall containing a yellow fluid, rich in fat, crystals and detritus.

This chain of events represents the type of cerebral degeneration which results from the closure of a fairly large vessel—the apoplectic stroke following the vascular accident of thrombosis. The other type is less frequent and represents a general rather than a local lesion of the cerebral blood vessels. Widespread disease of all or of great portions of the cerebral vessels may be found—an extensive obliterating endarter-

itis which affects especially the smaller vessels and produces relatively insignificant isolated degenerated areas, but which in the aggregate represents a most extensive change in the brain. The intimal changes result in a gradual reduction in the lumen of the blood vessels until the free passage of blood is so much interfered with that spontaneous clotting takes place, with the production of miliary areas of softening.

Thrombosis seems to be much more frequent in the male sex. Age is an important factor; thrombosis rarely occurs before the fourth decade, increases in frequency through the fifth and sixth decades, and after that is a predominant factor in cerebral vascular disease. The extensive use of alcohol or tobacco, exposure to phosphorus, lead or other metallic poisons, syphilis and nephritis in their destructive action on the blood vessel wall, general systemic diseases such as diabetes, gout, chlorosis, the acute infectious diseases and the puerperium, leukemia, etc., in their effect on the viscosity and coagulability of the circulating blood, play an important part. Debilitating diseases such as tuberculosis and neoplasms, by reducing the force and activity of the blood stream conduce to local slowing of the blood in the vessels and hence predispose to thrombosis.

The etiologic factors operative in producing the disseminated arterial disease, which results in the slow, progressive closure of the smaller vessels, are those that are considered responsible for general arteriosclerotic conditions elsewhere: nephritis, syphilis, exogenous and endogenous toxemias, excessive mental and physical exertion, etc. The condition may be a part of a generalized arteriosclerosis or may be limited to the cerebral blood vessels.

SYMPTOMATOLOGY

Different clinical manifestations result from the two types of vascular disturbance mentioned. The symptomatology may therefore be more or less definitely divided under two subheadings: (1) the abrupt or local type, and (2) the progressive or widespread type.

The Abrupt or Local Type.—As a rule, the onset in the abrupt type is not so sudden or apoplectiform as in cerebral embolism and cerebral hemorrhage. There are often prodromal symptoms, the nature of which depends on the location of the vessel involved; and there is usually some evidence of progression in the course of the symptomatology. Headache may be a prodromal symptom, usually intensified by coughing, straining or dependent positions of the head. For a number of months the headache may take the form merely of a sense of oppression, a feeling of "expansion of the intracranial contents," buzzing in the ears or a pulsatory sensation connected with the dilatation and contraction of the

vessels within the cranial cavity. Insomnia or drowsiness may also be one of the premonitory symptoms of this type of vascular insult.

At the time of the complete closure of the vascular channel the true symptoms of the cerebral thrombosis appear. There may be a sudden disturbance in consciousness, which may be either maximal or minimal in severity and in duration. If the area involved be large, consciousness may not return, and death may ensue without recovery from the initial attack. In the majority of cases, however, there is no actual loss of consciousness at the time of blocking of the vessel, but usually a period of slight or well marked confusion during which speech and thought associations are interfered with so that for a time the individual shows apparently a considerable reduction in his mental faculties. The confusion may take on an excited character, so that the patient may have a mild delirium or even an acute mania. Occasionally the state of excitement is characterized by mild or severe ideatory or sensory hallucinations. In many instances cerebral arterial thrombosis occurs at night and during sleep, at the time when there is a physiologic depression in the blood pressure and a reduction in the activity of the cardiovascular musculature.

Immediately following the initiation of the symptoms that result from the actual thrombosis, there is usually a period during which the disturbances are slightly or moderately progressive. If the motor area is mainly involved, for example, the initial symptom may be a monoplegia which after a time becomes a hemiplegia. Pain and tenderness of the skull overlying the areas of degeneration occasionally appear, and there may also be pain referred directly to the face, either limited to one or another subdivision of the trifacial area or to the entire trigeminal distribution. This is generally supposed to be due to an irritation of the dura mater and the other cerebral envelops which receive nerve supply from the fifth cranial nerve, the pain being referred to the cutaneous distribution of that nerve.

After the acute onset, there usually occurs an interval during which little alteration takes place in the symptomatology. In not a few instances, progressive recovery may ensue with a return of function which may be almost complete with an entirely satisfactory restoration of all the faculties and with only slight residual clinical evidence of any antecedent motor or sensory disturbance. Ordinarily there remains a certain residuum of disturbance of the motor or general or special sensory functions of the affected area, which may vary from a slight defect, observable on examination only, to more marked disorganization of function.

The Progressive or Widespread Type.—The second type of cerebral degeneration from obstruction to the circulation has a rather different

clinical picture, characterized, after the onset, by the progressive or remittent character of the course of events. With the slowly progressive diminution in the caliber of the vessels, the onset is ingravescent in comparison to that which has been described under the abrupt type. The same prodromal symptoms are observed, but the further course varies considerably. In place of the more or less sudden appearance of disturbances in the motor, sensory or psychic spheres, the interference with the physiologic functions of the cerebral cortex takes place much more slowly and has a progressive, intermittent or remittent character. The sensations of dizziness, fulness and heaviness of the head, etc., which characterize the prodromal period, become more and more prominent. Sensory symptoms develop: paresthesias, stiffness and pains referred to various portions of the body, either to one extremity or to the entire hemisomatic distribution, together with more or less transient, frequently repeated attacks of weakness of the face or of a hand or leg, often ushered in by dragging of the leg with clumsiness in the finer movements of the hand and fingers. Motor weakness is often associated with twitchings or sudden spasmodic movements of the face or extremities. These frequently tend to increase, until there are jacksonian or generalized epileptiform attacks, which are accentuated under all conditions of stress or under the influence of any factor that tends to depress the cardiocirculatory tone. There are often paraphasic disturbances, which gradually increase until a more or less clear-cut aphasia results.

The entire course of this symptom picture is characterized by its variability, the motor and sensory symptoms appearing, advancing, then regressing and in turn again undergoing a period of accelerated development. Finally, with the complete occlusion of one or another of the small arteries affected, the motor and sensory disturbances become permanent, with the development of a monoplegia, a hemiplegia, cortical disturbances in sensibility, a hemianopia or some other evidence of cerebral involvement. The psychic faculties also show a progressive diminution in function. The mental disturbances usually develop as a steady reduction in the intellectual capacity of the individual, with gradual loss of memory, particularly for recent events. These slowly increase in intensity and result in a progressive deterioration of the personality and the final syndrome of senile dementia. Sudden lacunar losses of memory may occur, with complete amnesia in regard to certain periods of the individual's existence and retention in full clarity of others. The progressive mental deterioration is usually accompanied by the evidences of extending degeneration in the motor and sensory areas. In this diffuse type of degeneration the symptomatology may be limited to one of the cerebral hemispheres, but there is often evidence of a bilaterality of involvement. With involvement of the frontal lobes

there may be marked alterations within the emotional field with outbreaks of forced laughter and weeping and the production of a more or less completely developed pseudobulbar syndrome. There is considerable difficulty in fixing the attention and a deficiency in judgment and reasoning. The patient may become irritable and impatient, and may develop marked motor and psychomotor activity necessitating constant care and watchfulness. Temporal and occipital lobe changes result in hallucinations of hearing, usually in the form of ringing in the ears, sounds of bells, gongs, trains, etc., while flashes of light and more or less formless visual hallucinations may result from the involvement of the occipital lobes alone. Evidence of disturbance in the rhinencephalic region is much less frequent, although gustatory and olfactory hallucinations may be observed.

The chronic progressive softening is ushered in with symptoms of irritation which later advances to paralysis, and the process may continue over many months or even years. While the condition is ordinarily encountered in persons of relatively advanced years, it may occur in early adult life, and it has been found in the new-born and described as "encephalitis congenita." When it occurs in infancy or childhood, the process is probably not due to an infection, but is rather a disease of the blood vessels on the basis of hereditary syphilis or (in older children) of alcoholism.

In either of the two types of cerebral degeneration described above, there may appear disturbances in the joints and in the muscles, such as are usually associated only with lower motor neuron paralysis. The trophic disturbances which occur in and around some of the joints are out of proportion to what might be ascribed to disuse, and the muscular atrophy may be as great as that seen in disease of the ventral horn cells or of the peripheral nerves. The trophic changes may be found in the muscles of the upper extremity, about the shoulder, in the arm and forearm, and particularly in the muscles of the thenar and hypothenar eminences and in the interossei. The explanation of these disturbances has been unsatisfactory; in the majority of instances they are supposed to be due to a loss of the trophic influence of the cerebrum over the ventral horn cells which supply the muscles and skeletal tissues.

In the motor disturbances occasioned by vascular degenerative changes, a partial monoplegia is more frequent than a total monoplegia, and disturbances are more frequent in the upper than in the lower limbs. On account of the anatomic arrangement of the ascending frontal convolution, certain types of motor disturbances have been described in connection with these vascular disturbances. Oppenheim has reconciled these definite types with the functional localization in the motor cortex as follows: (1) a crural monoplegia which usually results from a lesion

of the paracentral lobule and the upper third of the ascending frontal convolution; (2) a faciobrachial type, in which the middle portion of the ascending frontal convolution is involved producing disturbance in the innervation of the face and of the arm; (3) involvement of the lower portion of the ascending frontal convolution with the so-called glossolabial type of motor disturbance, in which the musculature of the face, tongue and soft palate shows a more or less marked involvement.

Cerebral degeneration, therefore, may be divided into two types, dependent on the anatomic character of the involvement—the first being the result of an interference with the permeability of a relatively large single trunk and characterized by a prodromal period followed by a relatively abrupt phase during which the symptomatology is more or less rapidly developed, followed by a period of restitution of function. This type is usually unilateral, affects certain definite areas of the cortex and is characterized by a relatively incomplete loss of function. The second type is characterized by the same prodromal period, but instead of an abrupt onset it develops more or less insidiously, with intermissions or remissions, continues to progress and shows definite evidence of bilaterality. The lesions are distributed almost uniformly throughout one or both hemispheres and result in the reduction of all the functional capacities of the cortex, with marked mental and emotional changes often resulting in either frank psychotic or definitely demented states.

The following two histories illustrate the clinical course in patients who on the operating table presented what is termed "cortical degeneration."

REPORT OF CASES

CASE 1.—*Cerebral symptoms of one year's duration. Exploratory craniotomy exposing large area of degenerated brain. Death one year later; necropsy.*

Clinical History.—Mrs. J. H., aged 50, married, American, a housewife, admitted into the New York Neurological Institute in 1922 as a private patient of Dr. Tilney, became ill in November, 1920, with pain in the back of the head on the right side, which extended forward over the right eye. It was present almost constantly, was subject to exacerbations and would continue until relieved by medication. It was entirely relieved by moderate doses of acetylsalicylic acid. Exposure to cold, especially riding in an automobile, made the pain much worse. It was not affected by sneezing, coughing or by moving about, and was so intense as to be incapacitating unless relieved by medication. The sinuses were examined, and nothing pathologic was found. She did not vomit, and had no dimness of vision or diplopia. During the summer of 1921, the headache ceased for a time. In November, 1921, the headache returned and spread over the right side of the head and down into the neck. One morning while dressing she found that her left hand was weak and that there was difficulty in using the fingers of the left hand, although she could move the arm, hand and fingers. This difficulty increased, and she had to be assisted in dressing. After a day or two the weakness disappeared, but the headache continued. During December, 1921, the weakness of the left arm returned and

slowly progressed. She could lift her arm, move it to a certain extent at the elbow, but she had no power in the wrist or fingers. About Jan. 8, 1922, there was an increase in all the symptoms, and she was confined to bed. A few days later roentgenograms of her teeth and sinuses were taken, which were negative. At that time she noticed that there was some numbness in the left hand. She had had no trouble with her lower extremities except for a certain amount of unsteadiness in walking, which developed about January 1. At the time of the second attack of paralysis of the left hand, her urine was found to contain albumin, and she was treated by colonic irrigations.

The patient had had no accidents, operations or injuries of any severe extent. Some years before she ran into a door and struck her head, the right side being injured, but she suffered no sequelae from that accident. She had had no pulmonary, cardiac or gastro-intestinal symptoms at any time. She had had measles and scarlet fever in childhood. In 1910 she had a sudden disturbance in consciousness. She felt very drowsy and was said to have fallen to the floor, with some frothing at the mouth. She was apparently "out of her head" for some hours, but had recovered completely by the following morning, although she felt as if there had been some memory defect and as if she had been away. In 1913, while abroad, after a rather long, strenuous walk she returned quite exhausted and fainted. In the autumn of 1918, she had an attack of syncope with nausea. On returning to consciousness she had no recollection of the events immediately following her syncopal attack, but this was not followed by any other disturbance. She was seen by a physician during this attack, but does not remember any diagnosis having been made. None of these attacks left any weakness, numbness or sequelae which were of sufficient severity to attract her attention.

The patient drank tea and coffee in moderation, did not use alcohol or tobacco, and slept well. Her appetite was good, her bowels moved regularly, and there had been no marked loss or gain in weight. She urinated once or twice every night. Her periods had been regular until her menopause two years before. She had had five children, whose ages range from 13 to 4 years, all living and in good health.

Physical Examination.—The patient was a poorly developed, fairly well nourished woman of about 50 years, lying quietly in bed and presenting a slight left facial weakness, which was evident both in repose and in movement. She did not move her left arm spontaneously, doing everything possible with the right hand and arm. Her walking showed the results of having been confined to bed, but presented no particular weakness or unsteadiness on either side. There was some swaying with the eyes open, not increased by closing the eyes, which seemed to be the result of general, not of focal weakness. The finger-to-nose test was performed normally on the right side, but was quite impossible with the left hand on account of the motor weakness. The finger-to-finger test was performed normally with the right hand, but was quite impossible with the left hand. The heel-to-knee test was performed normally in the right leg, but presented a certain amount of ataxia and unsteadiness in the left leg. In attempting to run the heel along the shin she succeeded very well with the right leg, but presented the same ataxia and wavering movement in the left leg. The toe-to-object-above-the-patient test was performed normally on the right side, but presented some weakness on the left side.

There was no dysmetria; she had no difficulty in making movements with the right hand, but efforts to test this on the left were impossible on account of the motor weakness. Movements intended to test the ability of the patient

to perform successive movements showed no impairment of cerebral function on the right side, but were impossible of performance on the left side on account of the motor weakness noted above. Skilled acts were performed normally on the right side, but could not be done with the left hand.

The tendon reflexes on the left side were more active than on the right; there was a left pectoral clonus. The abdominal reflexes could not be elicited, and there was a Babinski, Chaddock and Schaefer sign on the left.

There were no abnormal involuntary movements. Movements at the left shoulder were weak, but the shoulder could be raised to a slight extent in all directions, and the arm could be raised forward, laterally, backward, abducted, adducted and rotated to a slight extent. The movement of the forearm on the arm presented extensive motor weakness both in flexion and extension. Movements of the hand on the forearm were entirely abolished, and there were no movements in the fingers of the left hand. There was some weakness in the lower extremities. Movements of the thigh on the pelvis, leg on the thigh, and the foot on the leg all presented definite weakness.

There was some atrophy of the left arm and finger muscles. The muscle tone was somewhat increased in the forearm and finger muscles. No abnormal associated movements could be elicited in tests made on the upper extremity.

General Sensory Examination: Perception of absorbent cotton was normal over the entire body. Tactile localization was considerably disturbed. Efforts to localize points stimulated on the surface of the left forearm and hand led to the production of errors about twice as extensive as those in locating similar points stimulated on the right forearm and hand. In using the two-point test it was found necessary to spread the points of the calipers about twice as far for tests on the left side as for tests on the right before the duality of stimulation was recognized.

Pain sensibility was essentially normal over the entire body, although the patient stated that the pin point was not quite so definite, was somewhat more diffuse and less easily recognized on the left hand than on the right. When the pin point was applied with the eyes open the patient said that there was apparently some delay in the detection of the stimulus when the left side was tested, which was not present on the right side.

Temperature sensibility presented the same disturbances as those outlined on examination of the pain sensibility.

Vibratory sensibility was normal throughout the entire body.

Muscle-tendon sensibility was normal in the entire body, with the exception of the left upper extremity. The disturbance in this type of sensibility was most marked in the fingers, less marked at the wrist and elbow and only slightly interfered with at the right shoulder.

The ability to recognize an object by its form and the ability to estimate and compare different weights was lost in the left hand.

Cranial Nerves: The sense of smell was normal.

The eyegrounds showed a slight blurring on the mesial side of each disk. Elsewhere the outline of the disk was sharp and distinct. No pallor was seen in the nerve head, and the media, retina and retinal vessels showed no abnormalities. The fields were complete.

The pupils were equal, about 3.5 mm. in diameter, round, regular in outline and central in position. The reaction of the pupils to light, both direct and consensual, and the reactions in accommodation and convergence were normal on the two sides. The palpebral fissures were equal on the two sides. There

was no ptosis or exophthalmos. Movements of the eyes were normal except for slight weakness of the right eye in converging, and there was no nystagmus.

The trigeminus nerve presented no abnormalities either in its sensory or in its motor portions.

There was some lagging and stiffness in the movement of the left occipitofrontalis and corrugator supercilii muscles. The left orbicularis palpebrarum muscle was somewhat weak. The musculature of the left nostril, upper and lower lips and left side of the chin was definitely paretic.

Examination of the auditory apparatus showed no abnormalities in either the vestibular or the cochlear apparatus. Bone and air conduction on both sides was found to be normal, and no disturbances were found on caloric stimulation of the semicircular canals.

The glossopharyngeal, pneumogastric, spinal accessory and hypoglossal nerves were all normal.

Systemic Examination: The pulmonary system apparently was normal. The heart was normal in position and outline, and there were no murmurs. The cardiac rate was 80; the blood pressure 130 systolic, 80 diastolic. The blood vessels, both arteries and veins, showed no abnormalities. The gastrointestinal, genito-urinary and skeletal systems were normal.

Blood examination revealed: hemoglobin, 90 per cent.; red blood cells, 5,200,000 per cubic millimeter; white blood cells, 8,500 per cubic millimeter; neutrophils, 77 per cent.; lymphocytes, 22 per cent.; large mononuclears cells, 1 per cent. The Wassermann reaction was negative.

The spinal fluid was clear, and under normal pressure; there were no cells, no excess of globulin, a normal amount of sugar. The Wassermann reaction and colloidal gold curve were negative.

The urine was turbid, acid in reaction; specific gravity 1.020, no albumin, no sugar, no indican, a few micro-organisms, scattered and clumped white blood cells and some calcium oxalate crystals. The phenolphthalein excretion was 27 per cent. in two hours. The Mosenthal nephritic test meal showed small quantities with a rather high specific gravity, with some tendency of the specific gravity to remain fixed. The excretion of urea and chlorids was normal.

At a staff conference, held Jan. 19, 1922, the diagnoses suggested were a vascular lesion, neoplasm or multiple sclerosis. The location of the lesion was considered to be probably the right parietal, supramarginal and angular gyri. The patient was observed until January 28, during which time there was no essential change in her condition. She required repeated doses of acetylsalicylic acid with the occasional addition of codein for her headache. She was in bed most of the time.

Operation.—The patient was operated on on Jan. 28, 1922. A right osteoplastic flap was turned down, exposing the right side of the brain from a point about 1 cm. in front of the rolandic fissure. The dura matter when exposed was normal in color, and there was no evidence of increased intracranial pressure. On opening the dura an extensive area of brain degeneration was found extending from behind the rolandic area backward into the superior parietal lobule. This area extended upward nearly to the mesial margin of the hemisphere, downward almost to the lips of the Sylvania fissure with an extension forward which passed over the rolandic fissure and involved the ascending frontal convolution in the area which is known to supply the right forearm and hand. This entire area was discolored, canary yellow, and was much softer in consistency than the normal brain which surrounded it. Scattered over the surface were thickened vessels, some of which appeared broken. Scattered

irregularly over the surface there were three or four cysts containing small collections of fluid, and at the confluence of the various sulci and fissures the pia-arachnoid was thickened and milky in appearance. The entire region presented the appearance of an advanced degeneration with cyst formation. The dura and superficial tissues were closed without further investigation, and no tissue was removed for pathologic examination.

Course.—The postoperative course was uneventful. Following the operation, the patient improved and was able to be about and attend to her housework; but about a year later, the paralysis reappeared, she began to fail rapidly, and died after a short illness which was not characterized by anything definite. Her brain was obtained at necropsy, and the distribution and character of the lesions are visible in the sketch and photographs (Figs. 1 and 2).

Fig. 1 (Case 1).—Area of degenerated cortex.

CASE 2.—*Cerebral symptoms of one year's duration. Exploratory craniotomy exposed degenerated brain. Recovery; alive after nine years.*

Clinical History.—Miss B. R., aged 39, a teacher, a patient of Dr. B. Sachs, was admitted to Mount Sinai Hospital Oct. 8, 1916, complaining of inability to speak fluently for nine months, weakness of the right arm for one year, headache for three months, and weakness of the right leg for six weeks. One year before admission, the patient noticed that the right arm felt weak, especially when she was writing. This weakness persisted. Three months later, while teaching, she was suddenly affected by inability to form words, and she had some confusion in uttering sentences. She found that she was able to read, but had difficulty in speaking. The difficulty in speech continued, and if anything, became worse. Sometimes she was able to recognize and name objects, at other times she could not do so. She was unable to hold any kind of conversation without frequent interruptions on account of the difficulty in expressing her

thoughts. Three months before admission she began to have headaches which recurred frequently and were always on the left side of the head. A month later the right lower extremity became somewhat weak, and at the same time she noticed numbness in both arms and legs.

Physical Examination.—Such extensive weakness of the right upper and lower extremities was present that the patient had difficulty in using them. The biceps, triceps and wrist reflexes were much more active on the right side; the knee reflexes were very active, the right more active than the left. There was a transient ankle clonus and a Babinski sign on the right. The cranial nerves were normal. The fundi were normal. The sensory examination showed some diminution of vibratory and muscle-tendon sense in the right upper extremity, but was otherwise negative.

The blood pressure was: systolic, 125; diastolic, 90. The blood examination showed: hemoglobin, 75 per cent.; color index, 0.8; red blood cells, 4,320,000

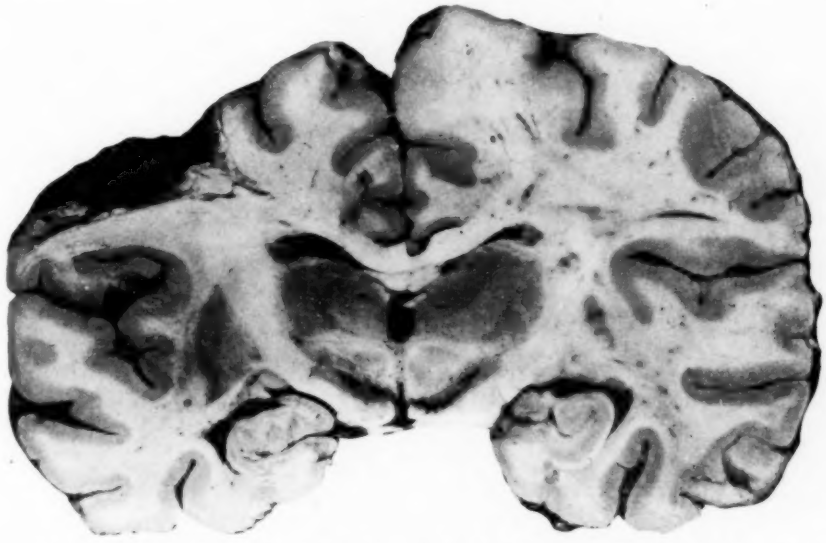


Fig. 2 (Case 1).—A section of the brain showing the involved area of cortex. Note that the size and relation of the bodies and inferior horns of the lateral ventricles are normal.

per cubic millimeter; white blood cells, 14,200 per cubic millimeters; neutrophils, 88 per cent.; small lymphocytes, 8 per cent.; large lymphocytes, 2 per cent.; eosinophils, 2 per cent.; slight anisocytosis and poikilocytosis. The Wassermann reaction was negative.

The spinal fluid was clear, under normal pressure; there were no cells; globulin content was normal; the Wassermann reaction was negative.

The urine was acid, the specific gravity 1.020; there was a faint trace of albumin, no sugar, a slight amount of indican and a few pus cells.

Operation.—An exploratory craniotomy was performed on Oct. 27, 1916. A large osteoplastic flap was turned down on the left side, exposing the parietal lobe and the motor area. The dura was not tense. When the dural flap was turned down, the cortex over the angular gyrus and the parietal lobe up to the median line as well as contiguous areas of the rolandic convolution were

yellowish and very soft. The pia-arachnoid seemed normal, and the portion of the brain that was involved was depressed below the rest of the cortex (Fig. 3). The dural flap was closed and the bone flap returned into place.

Course.—The patient recovered satisfactorily from the operation, and her headache disappeared. During the course of the following nine years, there was no recurrence of the headaches, and there was considerable improvement in speech. The weakness of the right arm and leg has persisted to the present time.

INFILTRATING CEREBRAL NEOPLASM

The course of infiltrating tumors of the cerebral hemispheres is so well known that a description of the general symptomatology is unnecessary. Although the subjective and objective neurologic disturbances

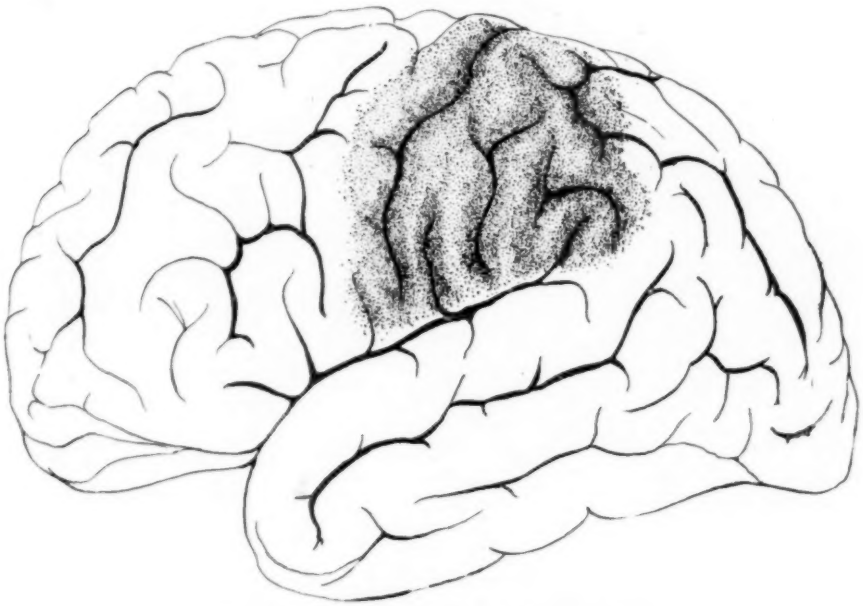


Fig. 3 (Case 2).—Area of degeneration.

vary with the location and the rapidity of growth, the general course is progressive, with, sooner or later, the appearance of signs of increased intracranial pressure. The remarks that follow have reference to those subcortical growths in which the symptoms present a certain similarity to vascular lesions.

In the earliest stages of infiltrating cerebral tumors, headache, vomiting and papilledema do not occur, and in not a few instances the signs of a rise in intracranial tension do not become evident for a long period. The brain often accommodates itself to the added foreign constituents, and by the substitution of neoplastic for brain tissue and the absorption of tissue fluids there is no appreciable addition to the total volume of the

intracranial contents. If the neoplasm is in one of the so-called silent areas—the right frontal or temporal lobe, for example—local manifestations may not appear for a long time, and only indefinite general symptoms are observed. It is not unusual for patients to present psychic deviations from the normal—gradual loss of memory, failure of the power to concentrate, alterations of personality, such as irritability, querulousness, drowsiness, apathy, loss of spontaneous speech, dissociation, sometimes stupor or psychotic states and other signs of marked mental deterioration. These patients are sometimes admitted into hospitals for the insane, and are for a long period supposed to be suffering from a mental disorder, until they finally develop signs of increased intracranial pressure, and the true nature of the disease is then recognized. In not a few of the patients, the correct diagnosis cannot be made or is only considered a possibility during life, but is made only at the postmortem examination when a deeply subcortical growth, which usually involves the corpus callosum, is discovered. Sometimes the mental disturbances are not so prominent, but the patients consult the neurologist on account of indefinite cranial symptoms, and for a long period the examination demonstrates few and vague neurologic disturbances. If such a person is past middle age, the diagnosis of cerebral arteriosclerosis, of progressive lacunar cerebral degeneration cannot be excluded.

Even when focal signs of cortical involvement appear, there may be no evidence of a rise in intracranial pressure, and in many of these patients, the differentiation between neoplasm and vascular change may be difficult. The symptoms of an infiltrating growth may have been dormant until a hemorrhage into the tumor has occurred, when definite and localized cerebral disturbances appear acutely. In these patients, the entire clinical course is almost similar to that of a vascular insult.

When, as occurs in many patients, signs of increase of pressure do appear, the differential diagnosis of tumor can be made with certainty.

During the past years, we have had under our care and treatment a number of persons with signs and symptoms of an intracranial lesion but without evidence of increased intracranial pressure; we were for a period in doubt as to the true nature of the lesion in not a few of the patients. In some of the patients, a puncture exploration of the brain as described by one of us has made possible a diagnosis of subcortical tumor; in others, the presence of dilated ventricles was determined by means of ventricular puncture, air injection and ventriculography which made it possible to differentiate between a vascular lesion and a neoplasm. In some patients, however, the diagnosis was "tumor or vascular lesion."

In comparing the symptoms and clinical course of infiltrating cerebral tumors and of progressive cerebral thrombosis, the main distinguishing features are the more steady advance of the disturbances and the appearance of symptoms of increased intracranial pressure in the former. The presence or absence of vascular disease cannot be depended on for the differentiation, for a general endarteritis and renal or cardiac disease may coexist with a tumor, and there may be no systemic blood vessel changes in thrombosis. All that can be said is that marked vessel changes and nephritis or cardiac disease make a diagnosis of a vascular lesion more probable. Nor is the bilaterality of symptoms and signs certain evidence that the disease is vascular, for not a few deeply subcortical tumors cause bilateral disturbances in the early stages of their growth. While the prodromal symptoms of thrombosis are very much like the vague disturbances often found in the early stages of an intracranial neoplasm, the onset of the symptoms of sudden closure of a large artery is more likely to be abrupt and the progress of loss of function more likely to be rapidly progressive. Even these features may, however, be misleading, for a rapid development of a hemiplegia from a subcortical new-growth is not at all unusual.

The early symptoms of the diffuse form of vascular disease also closely simulate the early symptoms of a slowly enlarging tumor in a silent area of the brain. In not a few of the patients, however, the signs of vascular disease in other parts of the body are so marked and the involvement of parts of the brain far distant from each other so distinct that the recognition of the lesion as a vascular one is probable.

INFILTRATING CEREBRAL NEOPLASM WITH CEREBRAL DEGENERATION

The possibility of a combination of vascular degeneration and an infiltrating neoplasm as the result of pressure or involvement of a larger blood vessel by the tumor has been described by many writers. A small amount of degeneration around a growth is not rare, and the occurrence of an extensive area of degeneration from involvement of a large blood vessel is not infrequent. If the amount of degeneration is small, the signs of the neoplasm—both the disturbance of function and the signs of increased intracranial pressure—may occur in the characteristic manner. If, however, the blood supply to a large area of the cortex has been interfered with, the signs of vascular degeneration may predominate, because the increase of cranial contents due to the tumor mass is compensated for by the diminution in size and the softening of a large amount of brain tissue, so that the sum total of intracranial contents is not above the normal. As a result there is no rise in intracranial pressure and therefore no papilledema. When the brain is exposed in such a patient, there is no evidence of increased pressure

within the cranial cavity, and a large area of the cortex is found to be yellow and softened, so that one would naturally conclude that the lesion was purely vascular. In the four patients whose histories are recorded in what follows, the symptoms, and course of the disease were like those of a vascular lesion, although a new growth could not be entirely excluded, and an exploratory operation was therefore performed. In two of the patients, exposure of an extensive area of changed and degenerated brain led the operator to conclude that the lesion was entirely vascular, but the subsequent course of the disease and more especially the appearance, months later, of papilledema and the other signs of increased pressure within the cranial chamber, led us to modify our diagnosis. The postmortem examination showed that the vascular change in the cortex was entirely secondary to a large infiltrating neoplasm which had compressed a large blood vessel. In one patient, the lesion was supposed to be vascular but the necropsy again showed that there was a large tumor. As the result of the experiences we had had, we concluded before the operation that one patient, who presented the clinical picture of a vascular lesion without the signs of increased intracranial pressure, had both a tumor and a vascular softening, a conclusion which was verified at the operation and subsequent necropsy. We have seen and operated in other cases of this nature, but they are not included in this report because the presence of a tumor was not verified by a postmortem examination.

REPORT OF CASES

CASE 3.—*Cerebral symptoms of ten months' duration. Exploratory craniotomy disclosed degenerated cortex. Death after five days. Necropsy showed deep subcortical tumor.*

Clinical History.—E. M., aged 36, an insurance agent, admitted to Mount Sinai Hospital as a private patient, Dec. 30, 1923, became ill in February, 1923, with difficulty in the use of a pen and progressive deterioration of handwriting, followed by the loss of the use of the right hand. In November, 1923, without any cause the patient suddenly experienced crying attacks, which were rather frequently repeated during the next month. Other evidences of emotional instability with some loss of initiative were also noted. In November, he first noticed weakness in the right upper extremity, and a short time after that, while bowling, he slipped and fell. The weakness persisted for several weeks and then gradually became worse. About the middle of November, he began to have difficulty with his speech, which progressed to such an extent that by the time of his admission to the hospital at the end of December, he was practically aphasic. During the twenty-four hours before admission, he had suffered from convulsive attacks, which had involved the right arm and the right side of the face, and spread to the right leg. The attacks were repeated as often as every fifteen to thirty minutes. He had not at any time complained of headache, but had vomited a few times during the preceding month. His wife stated that for several months before the weakness in the patient's arm appeared, he had been unusually irritable.

Physical Examination (Dec. 31, 1923).—The patient was drowsy; he seemed to understand everything that was said to him but was unable to reply. During the examination, a convulsive attack occurred in which the right arm was involved and later the right side of the face and the right leg. There was no loss of consciousness. There was complete paralysis of the right upper and lower extremities, with some spasticity but without sensory changes. The reflexes were uniformly increased on the right side of the body, with a double Babinski and double Chaddock sign. The fundi were normal except for a slight indistinctness in the margins of the disks due to a high degree of astigmatism. There was a right lower facial paralysis, and the tongue deviated slightly to the right. There was slight rigidity of the neck and a slight Kernig sign. There was marked tenderness on pressure over the left anterior temporal region.

The laboratory examinations were negative.

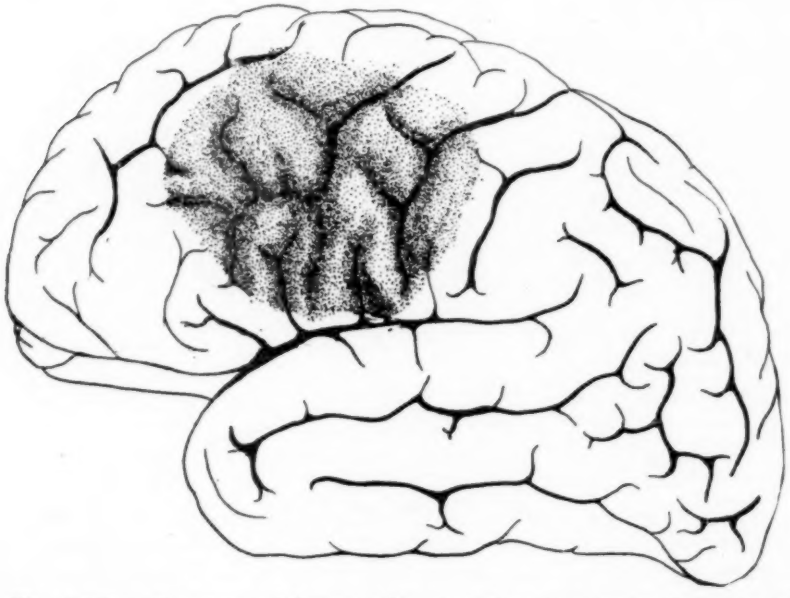


Fig. 4 (Case 3).—Area of degeneration secondary to a tumor (compare with Fig. 5).

Operation.—On Dec. 31, 1923, the patient was operated on, a left-sided craniotomy being performed under local anesthesia. The cortex exposed by the craniotomy appeared yellow and softened (Fig. 4), and the tension of the brain seemed slightly increased, but no evidence of a neoplasm was found.

Course.—The patient died on the fifth day after operation with hyperpyrexia.

Necropsy.—Necropsy revealed: a recently sutured "U-shaped" wound of the scalp and a corresponding bone flap beneath and under the flap a moderate amount of recent extradural hemorrhage. The surface of the brain showed evidence of increased intracranial pressure, the sulci were shallow and the gyri flattened. On separating the hemispheres a distortion of the corpus callosum by a tumor projecting through it was seen. The left side of the brain appeared to be larger than the right.

On section of the brain a large infiltrating tumor of the left frontal lobe was seen (Fig. 5). The tumor extended forward to within 5 cm. of the anterior pole and 4 cm. from the lateral margin of the brain. It invaded both sides of the corpus callosum at the genu and for a short distance caudad. The tumor measured about 8 by 5 by 4 cm. It was yellowish red on fresh section and not encapsulated. There were a few streaks representing the sites of operative punctures, a few areas of fresh hemorrhage surrounding them. The pathologic diagnosis was spongioblastoma.

CASE 4.—*Cerebral symptoms of three months' duration. Exploratory craniotomy showed degenerated brain. Recovery. Advance of symptoms with papilledema. Death after two months. Necropsy showed large subcortical tumor.*

Clinical History.—Mrs. H. R., aged 43, a school teacher, admitted to Mount Sinai Hospital as a private patient of Dr. I. Wechsler, during the latter part of

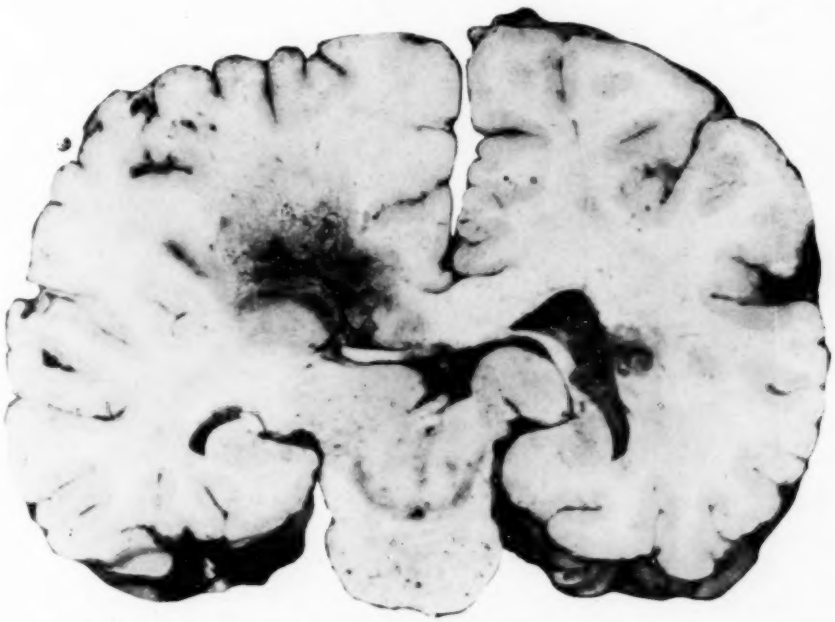


Fig. 5 (Case 3).—A section of the brain showing the location of the subcortical infiltrating growth. Note the dilatation of the contralateral ventricle.

November, 1922, first noticed attacks of fatigue which would come on rather suddenly and last for several hours. During these attacks she would have to lie down and rest. Afterward she would feel perfectly well. They were not sufficient to cause her to give up her occupation. About Dec. 1, 1922, she experienced a sensation of numbness in the fingers of the right hand and also in the remainder of the right upper extremity. This condition was transitory.

One day, in the latter part of December, the patient was found in an hysterical state, laughing and weeping and stating that she had had a stroke and was becoming paralyzed. She had observed a flattening of the lower part of the right side of the face and weakness in the right upper and lower extremities. There was no speech disturbance at this time. She remained in bed for a few days and then was allowed to be up, but was unable to stand alone

and could walk only with assistance. Three or four days after the acute onset she noted some disturbance in her speech, with inability to find the word she wished to use. This disturbance in speech became progressively worse. She would frequently use the wrong word, and then on suggestion use the correct one. She was finally forced to limit her conversation to short sentences, making herself understood with considerable difficulty. She said that she could not put her ideas or wishes into words and was unable to state them. Mentally she could name any object shown to her but she was unable to pronounce the name. She called many people by the wrong names, recognizing at once that she had made a mistake. At the end of the week she found that reading was difficult. The motor weakness of the right upper and lower extremities had become progressively worse. She had had no headache or impairment of vision and had not vomited.

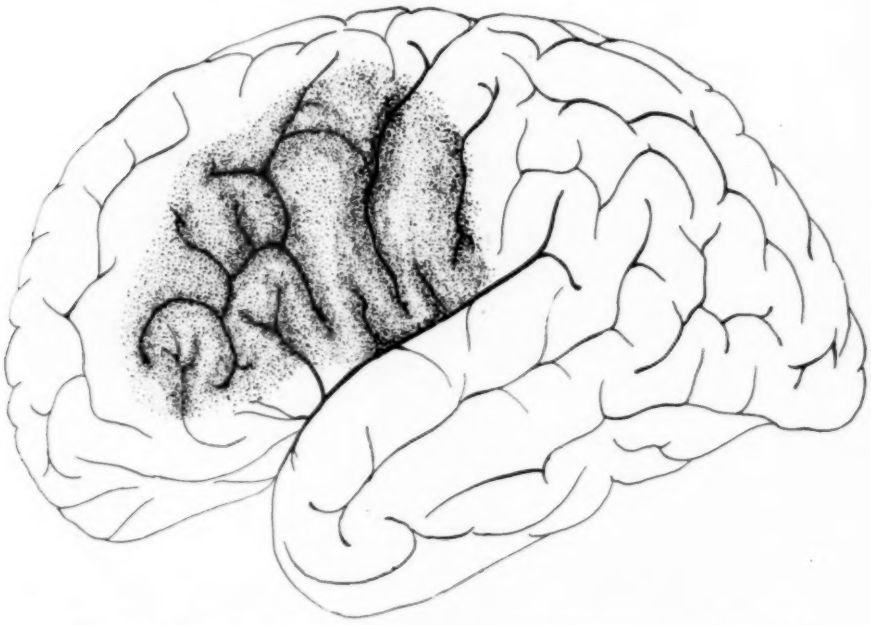


Fig. 6 (Case 4).—Area of degeneration. (Compare with Fig. 7.)

Physical Examination (Jan. 17, 1923).—The patient had a typical right hemiplegic gait, with practically complete motor paralysis of the right upper extremity. The fingers of the right hand showed some spasticity. The right lower extremity was very weak, but all movements could be carried out. The left side of the body was normal. The reflexes showed a slight relative increase on the right side, with a Babinski sign and its modifications. Pain sensibility seemed to be less on the right side of the body, and the vibration of a tuning fork was felt less well on that side. Joint sense was lost in the right hand, wrist and elbow, and in the toes of the right foot. There was total astereognosis in the right hand. There was slight engorgement of the retina with haziness of the right disk. The oculomotor apparatus was normal, except that there was a slight nystagmus. Some diminution in pain sense was present over the right side of the face, with supranuclear paralysis of the right facial nerve.

Mentally, the patient was fairly normal, but with some tendency to ramble and to introduce irrelevant statements on account of the aphasia. She was unable to complete sentences but could use short phrases fairly well. She was aware of the word she wished to use but could not conjure it up at will. She understood the use of objects and nodded her head when the correct name for an object was used. She understood written or printed language. She was able to write imperfectly with the left hand.

The blood pressure was 120 systolic, 74 diastolic. The laboratory examinations showed nothing abnormal.

Operation.—At operation, on Jan. 26, 1923, a large softened area, caudad to the rolandic fissure, including most of the parietal lobe, was found (Fig. 6).

Course.—Two days after the operation there was a sudden onset of stupor, which was interpreted as being due to a hemorrhage into a subcortical neoplasm. The patient's condition varied considerably; she was stuporous most of the time, although at intervals she would recover consciousness. There was continual incontinence. The diminution of pain sensibility over the right side of the body became more distinct.

Fig. 7 (Case 4).—A section of the brain showing the location and size of the subcortical growth. Note the dilatation of the contralateral ventricle and the approximation of the vertical planes of the body and inferior horn of the ventricle.

By March 1, a bilateral papilledema of 3 diopters had appeared, with slight hemorrhages and patches of exudate. She gradually became comatose, developed signs of hypostatic pulmonary congestion, and died March 19, 1923.

Necropsy.—Postmortem examination showed a large infiltrating tumor involving the region of the left basal ganglia (Fig. 7). The tumor was deeply

placed and adjacent to the body of the lateral ventricle. In the body of the tumor there were a few small areas of hemorrhage. Microscopic examination showed it to be an infiltrating glioma. The upper portion of the left frontoparietal and temporal lobes from the vertex down to the tumor were found to be much softer than normal and somewhat yellowish.

CASE 5.—*Cerebral symptoms of one year's duration. Exploratory craniotomy showed tumor and degenerated brain. Death; necropsy.*

Clinical History.—H. M., aged 40, a mail-carrier, admitted to the Neurological Institute as a private patient, for three years prior to admission complained of occasional right frontal and temporal headaches, which might occur about once a week and would last for two or three hours. In April, 1923, the patient experienced a sudden attack of loss of consciousness which lasted for about fifteen minutes, during which the head, the mouth and jaws were drawn to the left, and the tongue was thick. Thereafter, similar attacks occurred every few

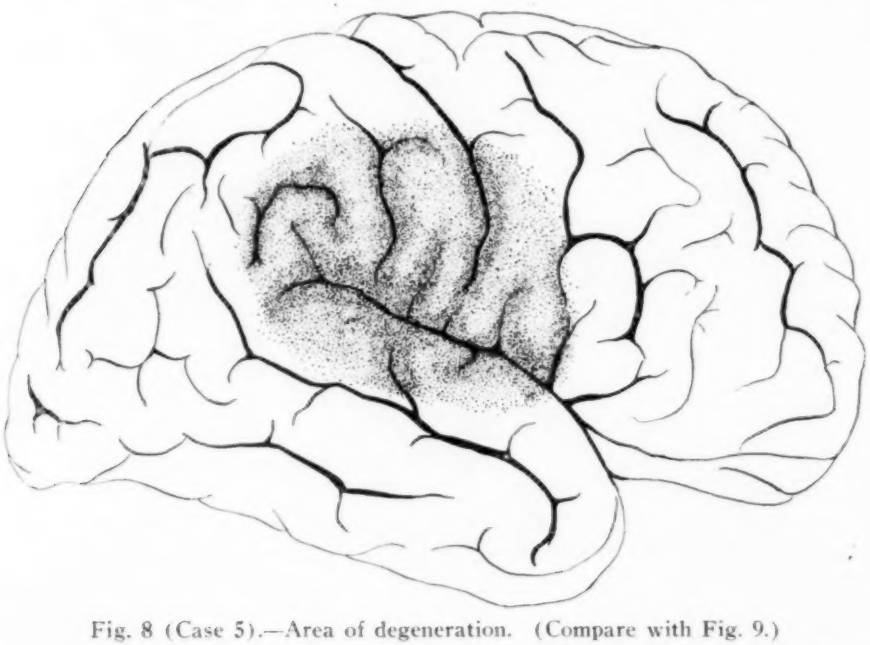


Fig. 8 (Case 5).—Area of degeneration. (Compare with Fig. 9.)

days. About five minutes before the attack he would have a peculiar sensation in his mouth and the tip of his nose, a pin and needle sensation in the tongue and a metallic taste in his mouth. About May 1, 1923, during one of these attacks, the left arm became numb, and this had continued. He would drop things from his hand, apparently from a disturbance in sensibility, and complained that he did not know where his arm and leg were in space. The headaches became more marked and were felt in both temporal regions. In April, there was some buzzing in the right ear. During the following month drooping of the left angle of the mouth and the left eyelid was first noticed, and the voice became whining. He had no disturbances in his legs and no trouble with vision. For many years the patient had taken from twenty to thirty cups of coffee and smoked about twenty cigarets a day. He was the father of one child, and his wife had had no miscarriages.

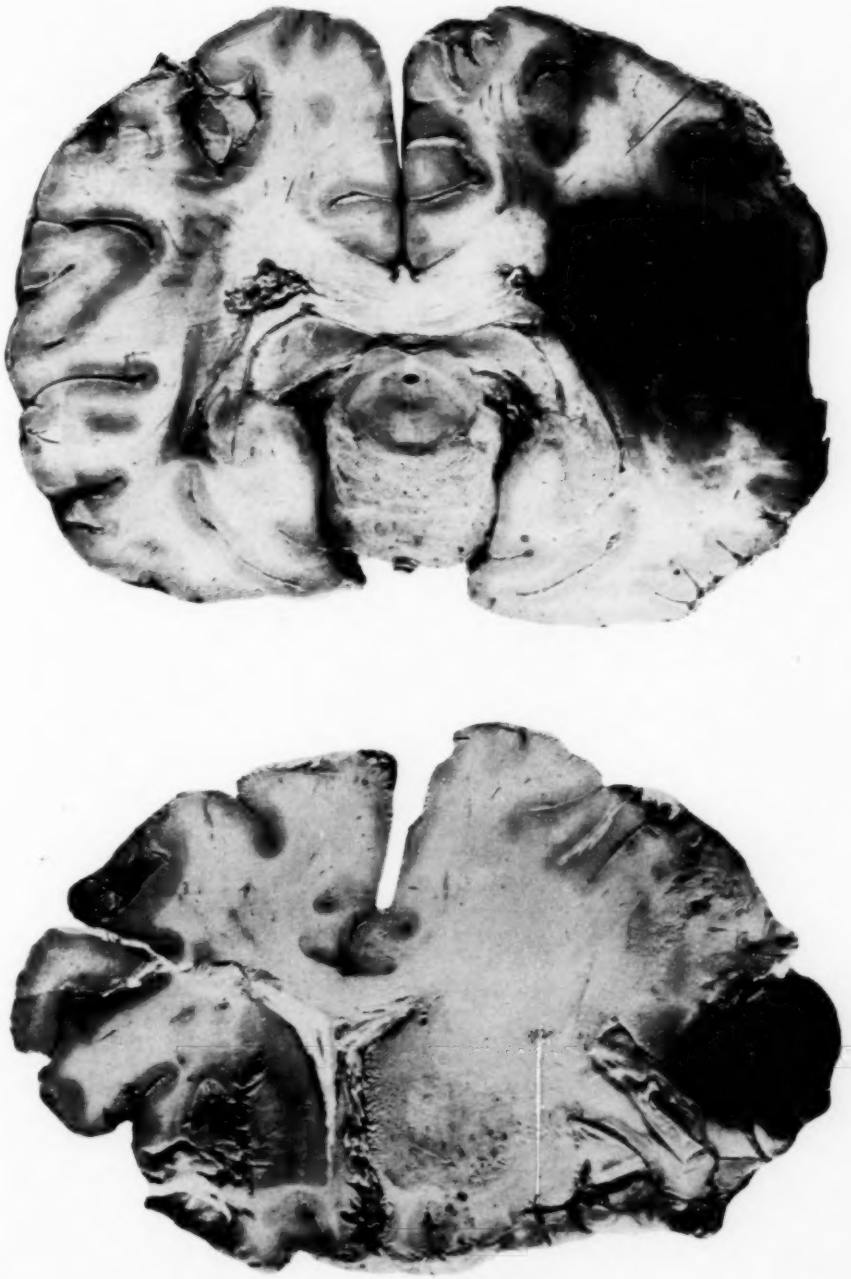


Fig. 9 (Case 5).—Sections of the brain showing the size and extent of the growth.

Physical Examination.—The patient was sluggish mentally and inattentive. His gait was normal. There was some intention tremor of both hands, more of the left than of the right. Considerable ataxia in the approximation of the left to the right finger. The finger to thumb test could not be performed with the left hand, although normally done with the right, with some dysmetria and adiadokokinesis in the left hand. There was some wavering and uncertainty in the use of the left lower extremity. The tendon reflexes were more active on the left side, and there was no plantar flexion of the left great toe on stimulation of the sole of the foot. The abdominal reflexes could not be elicited. There was weakness in the left upper and lower extremities. No finer movements could be made with the left hand, and there was some objective weakness of the left lower extremity. There was slight atrophy of the small muscles of the left hand. There was some hypertonicity in the left upper extremity. Tactile sensibility was diminished in the left hand and arm, and tactile localization and

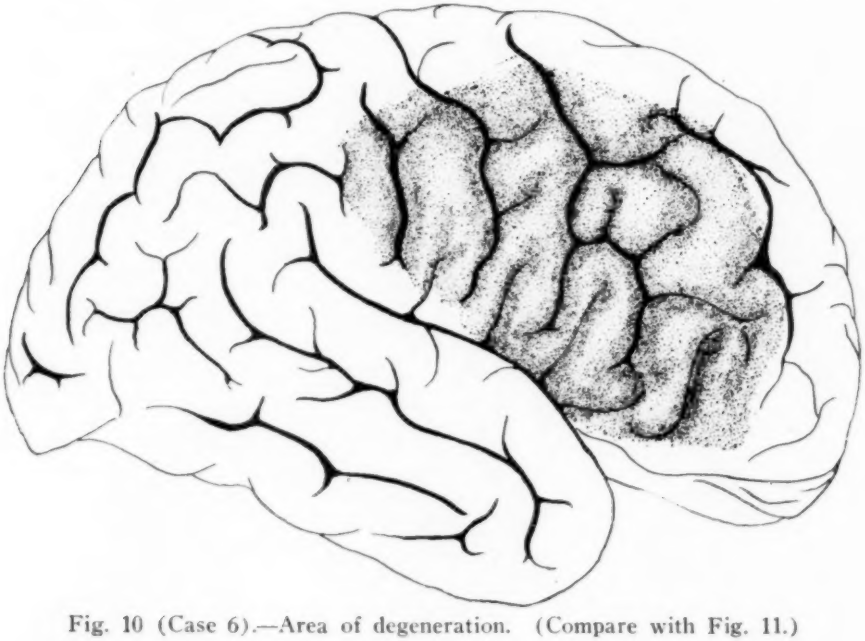


Fig. 10 (Case 6).—Area of degeneration. (Compare with Fig. 11.)

discrimination were also much involved, but pain, temperature and vibratory sensibility were normal. Muscle tendon sensibility was lost in the left hand, and there was an astereognosis.

The fundi were normal. The pupils were somewhat irregular, the left larger than the right; there was slight diminution in movement of the left eye toward the left, and a fine nystagmus on lateral gaze. The left seventh nerve showed a paresis of the upper branches and paralysis of the lower portion of the facial musculature. The left side of the tongue seemed to be flattened.

The blood pressure was 130 systolic, 80 diastolic. The laboratory examinations were normal.

Operation.—A right-sided craniotomy was performed. The intracranial pressure was somewhat increased. On opening the dura, an apparently infiltrating tumor was found in the region of the right Sylvian fissure at about the

middle of the horizontal arm of the fissure. The cortex of the frontal and parietal lobes situated dorsal to this neoplasm was yellowish and somewhat soft to the touch.

Course.—There was no improvement after the operation; the man recovered consciousness but grew gradually weaker and died a few days after the surgical exploration.

Necropsy.—Postmortem examination showed an infiltrating tumor at about the junction of the cephalic and middle third of the right Sylvian fissure which had compressed the branches of the right Sylvian artery to the ascending frontal and parietal convolutions, the superior parietal lobule and the superior temporal convolution. These areas showed marked softening together with a yellowish discoloration and fresh hemorrhages (Figs. 8 and 9).

Fig. 11 (Case 6).—Section of brain showing location and size of the subcortical tumor.

Microscopic examination of the tumor mass showed it to be an infiltrating glioma. Sections of other portions of the cortex showed the typical findings of a cortical degeneration.

CASE 6.—*Cerebral symptoms of four weeks' (?) duration. Exploratory craniotomy showed degenerated and softened brain. Death six weeks later. Necropsy showed large subcortical tumor.*

Clinical History.—Miss C. B., aged 47, unmarried, admitted to the service of Dr. Foster Kennedy at the Neurological Institute, had arrived in this country a few weeks before admission to the hospital, and no good account of her illness could be obtained. She had always been well until four weeks before

admission. Then she began to suffer from headache, became rapidly more and more drowsy, and lost more and more power in the left upper and lower extremities. On admission to the hospital, she was in stupor with incontinence of urine and feces. She could be aroused with difficulty, but when awake, she was well oriented.

Physical Examination.—This was difficult on account of the lack of cooperation. The left upper extremity was spastic and flexed at the elbow, the left lower extremity was spastic and the foot was held constantly in extreme plantar flexion. The biceps, triceps, radial, ulnar, patellar and Achilles' reflexes were much more active on the left. There was no ankle clonus, but a Babinski sign was present on the left. The abdominal reflexes could not be elicited.

Sensory examination was unsatisfactory on account of the lack of cooperation.

The fundi were normal except for a slight cloudiness of the right disk. The right pupil was larger than the left, and both pupils reacted sluggishly to light. The movement of the eyeballs could not be examined. The left cheek puffed out on expiration and the left eyebrow was at a higher level than that of the right side. As far as could be determined, there were no other cranial nerve disturbances. The heart action was slow and regular, with a systolic murmur at the apex. Examination of the blood and cerebrospinal fluid was negative. The roentgen-ray examination gave no diagnostic evidence.

The diagnosis lay between a vascular degeneration and a right frontal tumor, and an exploratory operation was decided on.

Operation.—Under local anesthesia, an osteoplastic flap was turned down exposing the right frontal and parietal regions. The dura was less tense than normal. When the brain was exposed, it was found to be yellowish, and the tension was less than normal. There was a large vein which ran an unusual course across the cortex of the exposed area. The lesion was considered a purely vascular one, the dura closed, the bone flap returned into place and the wound closed.

Course.—The patient recovered satisfactorily from the surgical procedure, but she became gradually weaker. She became emaciated, developed a complete left hemiplegia and died Nov. 17, 1923, six weeks after the operation.

Necropsy.—Postmortem examination showed that the patient had a large infiltrating glioma in the right frontal and parietal lobes overlaid by an extensive area of softened and degenerated cortex (Figs. 10 and 11).

These four cases are typical of the condition which we discuss in this article. The patients all were persons in the middle decades of life, who on a background of apparently good health slowly developed symptoms of organic cerebral disease characterized by both motor and sensory disturbances. The motor manifestations presented both irritative and paralytic phenomena, this also being the case with the sensory disturbances in which paresthesia appeared coincidentally with apparent diminution in sensibility. Mental changes were apparent in all of the patients. In none of the four were the cardinal symptoms of increased intracranial pressure—headache, vomiting and choked disk—observed to a degree considered sufficient to make the preoperative diagnosis certain.

The differential diagnosis in each case lay between vascular degeneration and neoplastic disease, and in view of the fact that a definite diagnosis could not be made in any case, each patient was subjected to exploratory craniotomy. In three of the patients, nothing except extensive cortical degeneration was found, while in the fourth, the tumor was exposed at the time of the operation, together with a large area of cerebral softening surrounding it and extending into the areas supplied by the blood vessels which the tumor had compressed. The presence of a deeply situated tumor was suspected in the cases in which no tumor was observed, but this suspicion was not made a certainty until in one case there appeared what was apparently a hemorrhage into the tumor, with marked accessions of the symptoms and papilledema, and in the others, at the postmortem examinations.

SUMMARY

The clinical signs of a purely vascular lesion, an infiltrating growth and a combination of infiltrating growth and vascular lesion may be almost similar, and the differentiation of one from the other conditions may be difficult.

In general, thrombosis of a cerebral artery is more likely to occur in persons with cardiovascular lesions or secondary to a systemic infection or wasting disease. Thrombosis is rare in the early decades of life, and the symptoms from the actual closure of the vessel are likely to appear suddenly.

If the thrombus forms in a large cerebral vessel, the symptoms are focal in character, and—after an acute onset—often improve rapidly. In the diffuse type of cerebral degeneration secondary to widespread disease of the cerebral blood vessels, the symptoms are often intermittent or remittent, but are generally slowly progressive. Psychic manifestations are frequent, and motor and sensory disturbances are, to a considerable extent, referable to both cerebral hemispheres and often to regions widely separated from each other.

Before the actual thrombosis or thromboses, there may be—in both forms—a prodromal period of months' and sometimes of years' duration, in which vague sensorimotor and psychic disturbances occur, which are like the early symptoms of many infiltrating cerebral growths, especially those that have started in a so-called silent area of the brain. Until the general signs of an increase of intracranial pressure appear or the signs of a progressive involvement of a localized area of the brain become distinct, the differential diagnosis may be impossible unless recourse be had to exploratory brain puncture, to puncture of the lateral ventricle, air injection and ventriculography or to an exploratory craniotomy.

Cerebral degeneration and softening with and due to an underlying infiltrating neoplasm may make its existence apparent by symptoms of slowly advancing vascular degeneration. The vascular change is in the main confined to one hemisphere and ordinarily to a part of one hemisphere which corresponds to the area of distribution of a large blood vessel. The symptoms often appear in persons below the age at which vascular degeneration might be expected to develop, and in those who have no evidence of cardiovascular pathology. The course is often more steadily progressive than that of diffuse vascular degeneration.

In our cases of a combination of the two pathologic processes, distinct signs of a generalized increase of intracranial pressure were missing for a long time. Without doubt, the cerebral softening gives additional space for the tumor growth without severe headache and papilledema, and the possibility of vascular degeneration from a deeply situated tumor should always be kept in mind.

If the symptoms and signs have been so localized that there is justification for the surgical exposure of a part of the brain by an osteoplastic craniotomy, the presence of changed and softened cortex does not mean that there is no tumor. Most of our patients in whom a surgical exploration was performed and such an area of degenerated cortex found turned out to have a subcortical growth to which the softening was secondary. It is well to remember in this connection that a dural endothelioma might, in rare instances, by obstruction of a large cerebral vessel cause similar extensive vascular changes, the symptoms of which might overshadow the actual tumor symptoms for a considerable period.

BRAIN REPAIR *

RICHARD B. WILSON, M.D.
BOSTON

I shall describe briefly the reaction produced in two general paralytic brains by punctures with sterile needles for the purpose of introducing arsphenaminized serum into the ventricles.

Pfeiffer,[1] studying puncture canals produced by sterile blunt needles, in an effort to locate brain tumors, stated that inflammatory reaction of the glia was never present, but that cicatrization was accomplished through pure connective tissue proliferation without the aid of glia. Tschistowitsch,[2] after studying the brains of dogs and pigeons from three to one hundred and thirty days after injury with a platinum needle, concluded that connective tissue elements of the pia and vessels play the chief rôles in the healing process; and that the part played by the neuroglia is insignificant, merely aiding in the formation of a sclerotic zone about the cicatrix by shrinking. In the brains of dogs receiving needle punctures, Penfield[3] after six days found fibroblasts, new vessels and "gitter" cells. Seven months after the injury, he found empty tunnels with neuroglia fibers forming the limiting membrane.

In the two cases forming the basis of this report the patients received ventricle punctures with a sterile blunt needle 1 mm. in diameter. The first patient received one puncture six days before death; the second received six punctures at intervals of from seven to eleven and a half months before death. The trephine openings were made over the right second frontal convolutions. The sections were stained with cresyl violet, Mallory's connective tissue stain and phosphotungstic acid hematin neuroglia stain.

In the first case the needle track was recognized in the gross as a yellow streak. Microscopically, two areas of reaction could be distinguished. These areas are schematically represented by Figure 1. The central zone (Fig. 1 *A*) was sharply demarcated because of the intensity of the cellular reaction, and measured 0.5 mm. in diameter (Zeiss micrometer). Small round cells predominated in this zone. A few macrophages were also present. Some of the macrophages con-

---

* From the Department of Neurosyphilis, Boston Psychopathic Hospital and the Pathological Laboratory of the Massachusetts Department of Mental Diseases.

1. Pfeiffer: Fortschr. der Med. **27**:24, 1909.

2. Tschistowitsch: Zeigler's Beitr. z. path. Anat. u. Path. **23**:321, 1898.

3. Penfield, Wilder G.: Meningocerebral Adhesions, Surg., Gynec. & Obst. **39**:803 (Dec.) 1924.

tained tissue detritus; others found in the region where red blood cells were numerous contained much brown pigment, and in the area of a small hemorrhage still others had red cell inclusions.

Studying macrophages in the brains of rats injured with hot and cold needles, Macklin [4] noted that they were conspicuous on the third and fourth days. They were smaller and more irregular in the early stages but contained relatively more fat, and on the sixth day many contained red blood cells. Next in predominance were "gitter" cells, together with considerable detritus, shadow cells and disintegrating cells. In some areas, especially in the cortical layers, red blood cells were numerous. In these areas connective tissue was seen filling in the

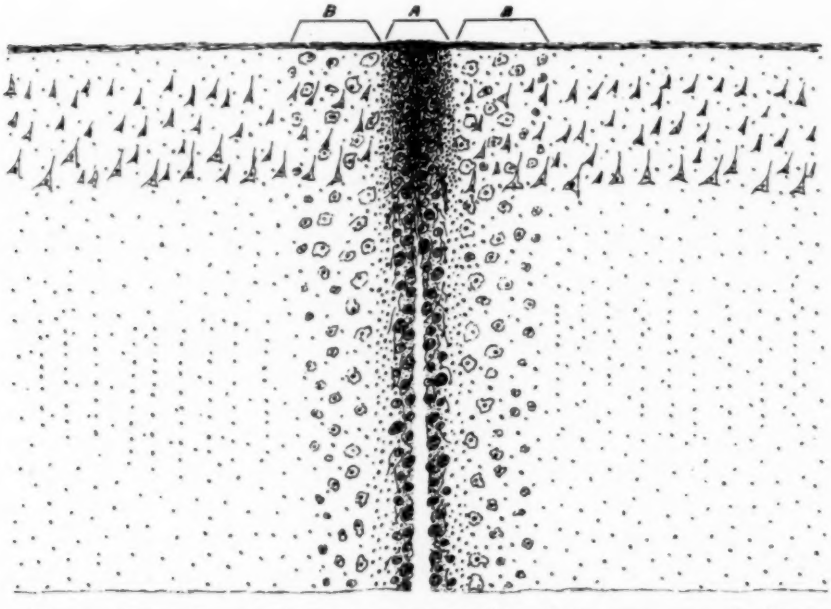


Fig. 1 (Case 1).—A schematic representation of the type and distribution of the reaction. *A* indicates the central zone of intense cellular reaction; *B*, the area of glial reaction manifested by increase of protoplasm.

lumen of the canal. Many delicate fibroblasts were found along the edge of the canal in close relation to small blood vessels. These also predominated in the cortical layers.

The variation in intensity of reaction at different levels was striking. In the cortical layers and the adjacent portion of the white matter, the reaction was most intense, and the lumen of the canal was here repre-

4. Macklin, C. C., and Macklin, M. T.: Study of Brain Repair in Rat by Use of Trypan Blue, with Special Reference to Vital Staining of Macrophages, Arch. Neurol. & Psychiat. **3**:353 (April) 1920.

sented by a narrow slit (Fig. 2). In the deeper white layers the cellular and connective tissue reaction was less intense and the puncture canal was still patent, measuring 0.28 mm. (Fig. 3). Detritus, shadow and disintegrating cells were more abundant. "Gitter" cells and macrophages in this area are seen in Figure 4.

The outer zone (Fig. 1 *B*) was characterized by many glia cells with large, round or oval, lightly stained nuclei, and with abundant

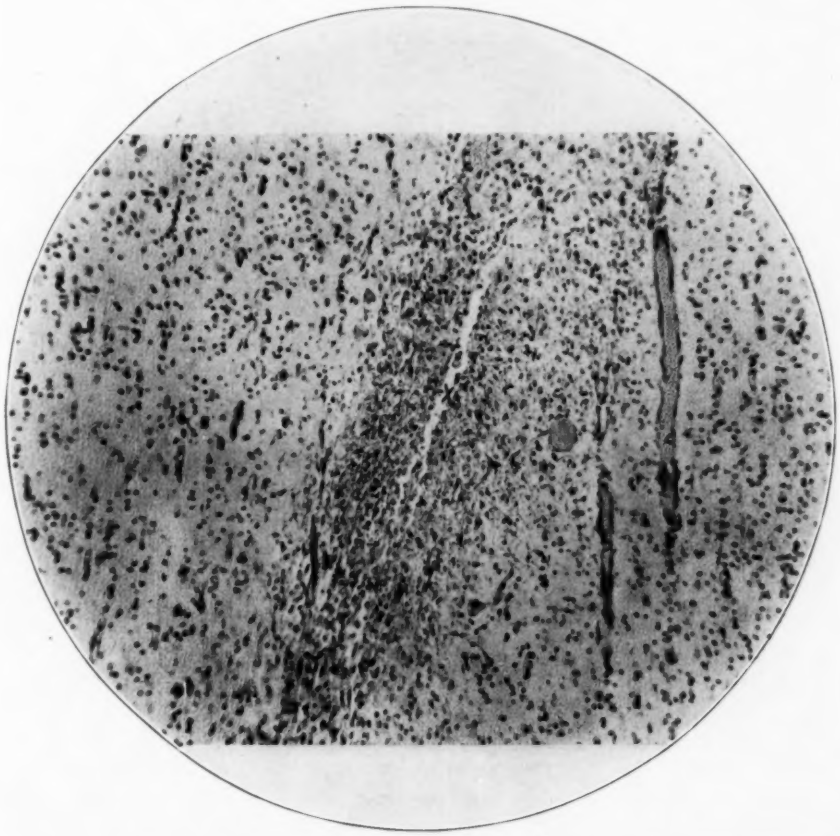


Fig. 2 (Case 1).—Wound canal at cortical and subcortical levels where the cellular reaction is most intense and the canal more nearly obliterated. Stained with cresyl violet; × 152.

protoplasm, the general contour of which was more or less regular, but many fiber-like processes gave the surface a ragged appearance (Fig. 5). An apparent increase in protoplasm of these glia cells was noticeable in the cortical layers 0.75 mm. from the central zone. The cells near the central zone had more protoplasm than those at the periphery. In this respect also there was a variation in different levels.

In the deeper white layers the appreciable increase of protoplasm could be recognized only 0.33 mm. from the central zone, and the protoplasm was less abundant.

In the second case, in which the needle track was at least seven months old, the cellular reaction was less intense; however, the same elements were encountered here as in the first case. There was also greater abundance of connective tissue. In the cortex the canal was fairly well filled in with connective tissue. Strands of it could be

Fig. 3 (Case 1).—Wound canal in deeper white layers showing patent canal and less intense cellular reaction. Stained with cresyl violet; × 110.

followed down from the pia (Fig. 6). In the adjacent white matter the canal lumen was filled in with loose strands of connective tissue in the meshes of which were many small round cells, macrophages loaded with brown granules, detritus, disintegrating cells, red blood cells and numerous "gitter" cells (Fig. 7). Deeper in the white matter the canals were less completely filled in. In one area at this level five tracks averaging 0.6 mm. in diameter were encountered very close together.

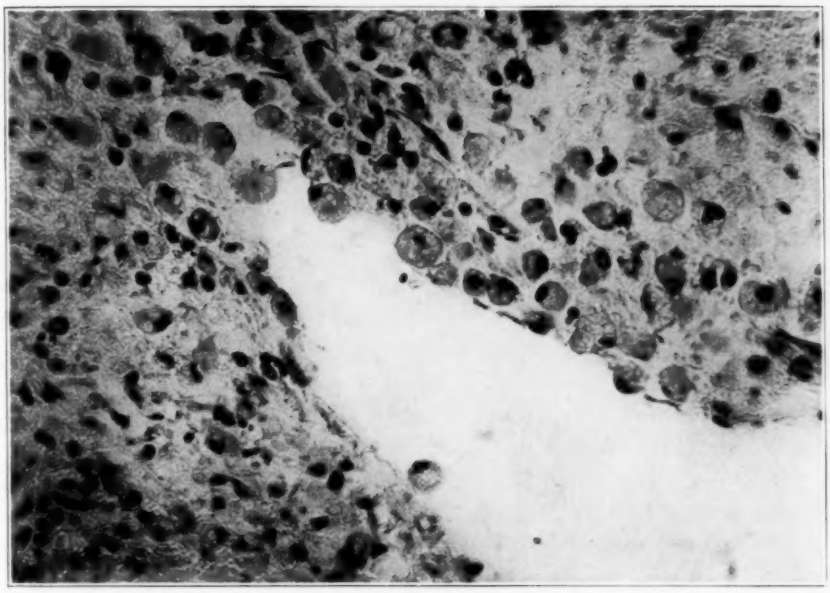


Fig. 4 (Case 1).—Deeper white layers showing phagocytic cells. Stained with cresyl violet; × 845.

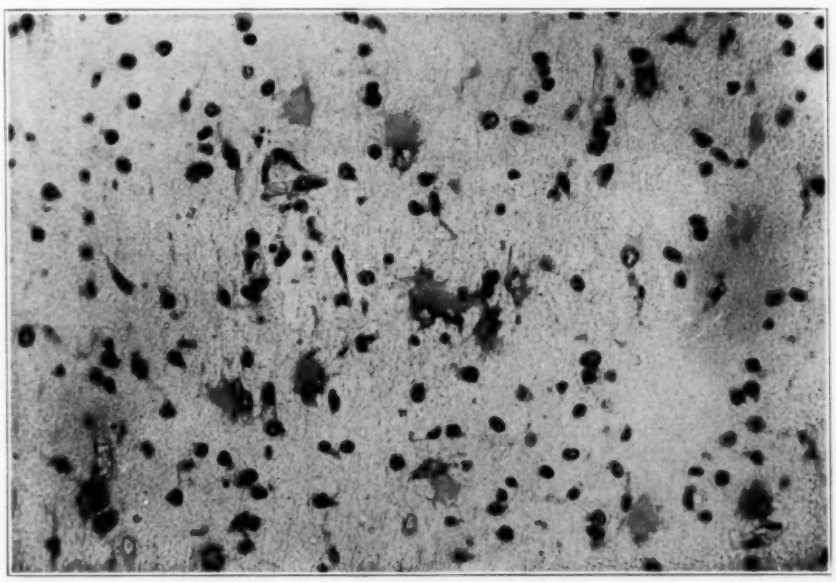


Fig. 5 (Case 1).—Glia cells, with increased protoplasm, found outside the central zone of intense cellular reaction. Stained with cresyl violet; × 740.

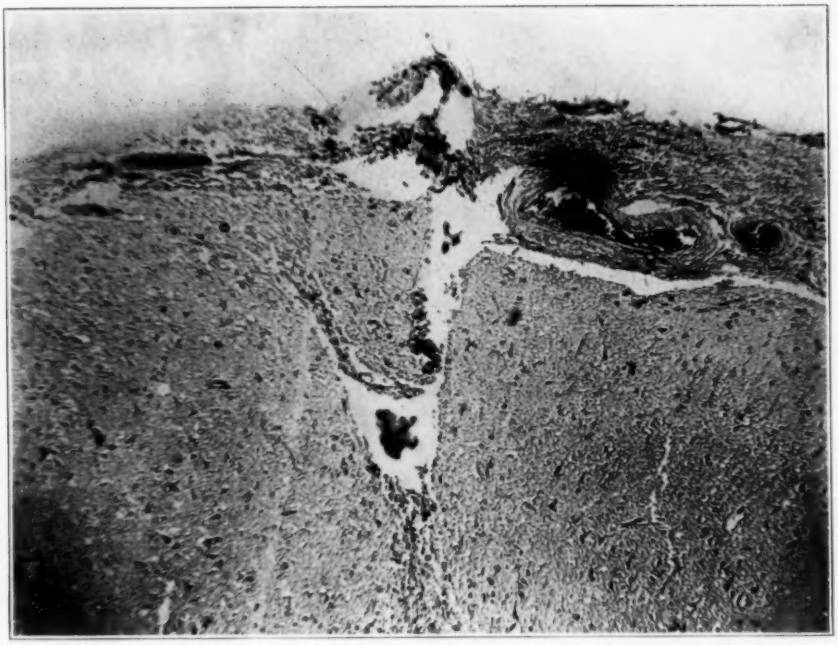


Fig. 6 (Case 2).—Sections through the pia and cortex. Connective tissue has almost filled in the wound canal. Strands of it can be followed down from the pia. Stained with Mallory's connective tissue stain; × 100.

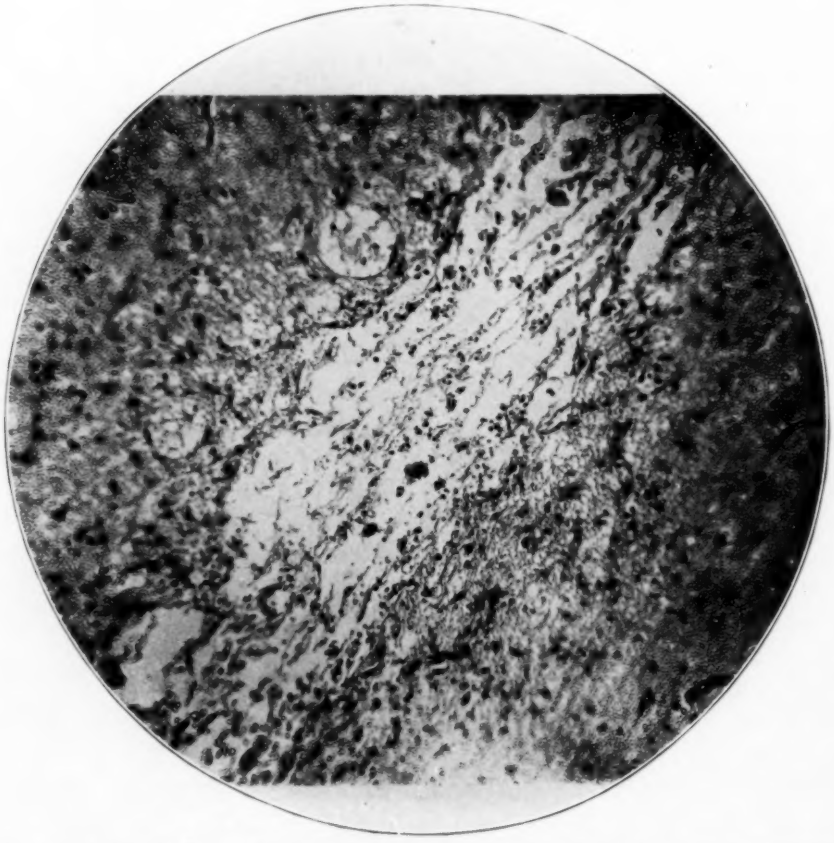


Fig. 7 (Case 2).—Section through the white matter adjacent to the cortex. Loose strands of connective tissue are seen in the canal. Stained with Mallory's connective tissue stain; × 155.

Between these tracks the white matter contained many clear spaces, giving it a chicken-wire appearance, so that the normal pattern of traversing fibers was entirely upset. This involved area measures 2.5 mm. by 4.8 mm. (Fig. 8). Most of the canals near the ventricle were filled in with connective tissue, including a few scattered neuroglia fibers (Fig. 9). Rare giant cells were encountered in this area (Fig. 10). On the surface of the ventricle at the point of entry a layer of rather densely packed red blood cells, including a few small, round cells and macrophages was found (Fig. 9). However, one canal entering the ventricle showed only loose strands of connective tissue and contained a great abundance of detritus, shadow and disintegrating cells, and macrophages, as well as many small round cells and "gitter" cells (Fig. 11).

The glial reaction in this case presents much the same appearance as in the first case; however, the beginning increase of protoplasm could be detected 0.5 mm. to 1.25 mm. from the cicatrix. A few cells contained large and small vacuoles, and an occasional cell contained pigmented granules or small round bodies. Nerve cells were not found in the central zone, but just outside, and did not differ in appearance from those elsewhere in the brain. A plasma cell was rarely found in the involved areas. In none of the canals did the neuroglia appear proliferated at the edge, forming a limited membrane; rather, the connective tissue elements seemed to blend with the neuroglia fibers at the edge. Then, too, the tissue bordering the canals contained numerous clear spaces in many areas, so that the density of the neuroglia increased as the uninvolved tissue was approached.

SUMMARY

The needle tracks in two general paralytic brains were studied, one six days after one puncture and the other from seven to eleven and a half months after six punctures. An attempt is made to describe the reparative process.

In the case in which puncture recently was performed, the cellular reaction was rather intense, especially in the more vascular regions. This consisted of small round cells, phagocytic cells and cellular detritus. The degree of the filling in of the wound canals appears to depend directly on the amount of vascularity of the tissue. It is accomplished by connective tissue elements. The connective tissue repair was more advanced in the older canals where rather dense connective tissue cicatrices were found, which blended with the bordering neuroglia fibers. In the deeper white layers the wound canals were incompletely filled in with loose strands of connective tissue, in the meshes of which were many phagocytic cells and considerable cellular detritus. Of inter-

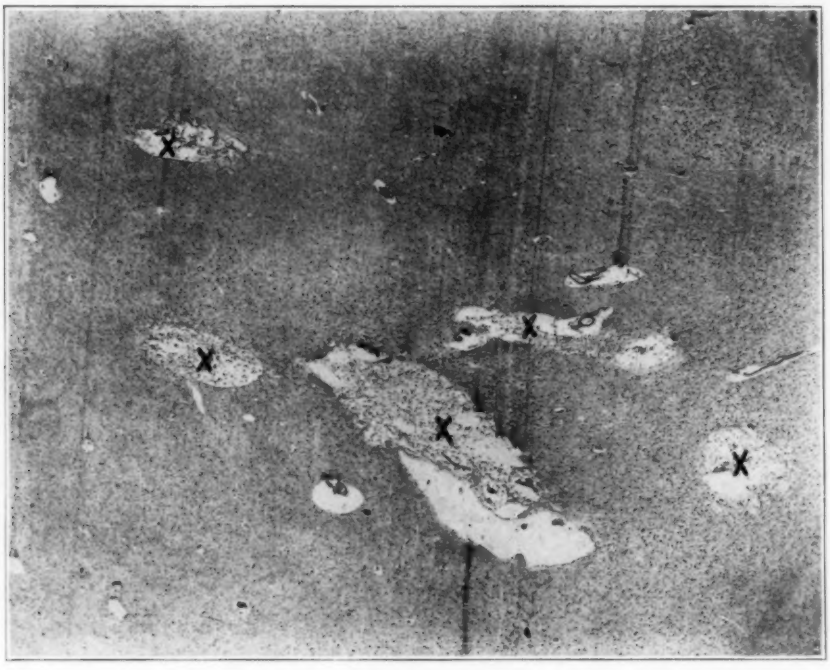


Fig. 8 (Case 2).—Appearance of the wound canals in the deeper white layers from seven to eleven and a half months after injury. *X* marks the wound canals. Stained with Mallory's connective tissue stain; × 25.

Fig. 9 (Case 2).—Section through ventricle. The dense connective tissue cicatrix is shown, also the layer of red blood cells on the surface of the ventricle. Stained with Mallory's connective tissue stain; × 60.

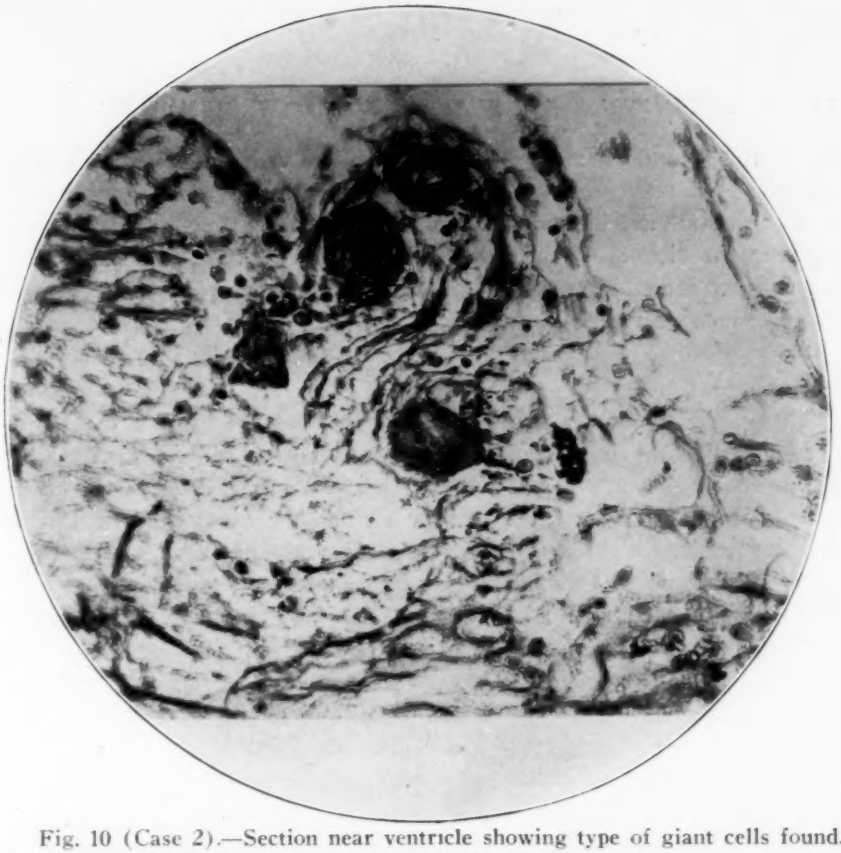


Fig. 10 (Case 2).—Section near ventricle showing type of giant cells found. Stained with Mallory's connective tissue stain; × 625.

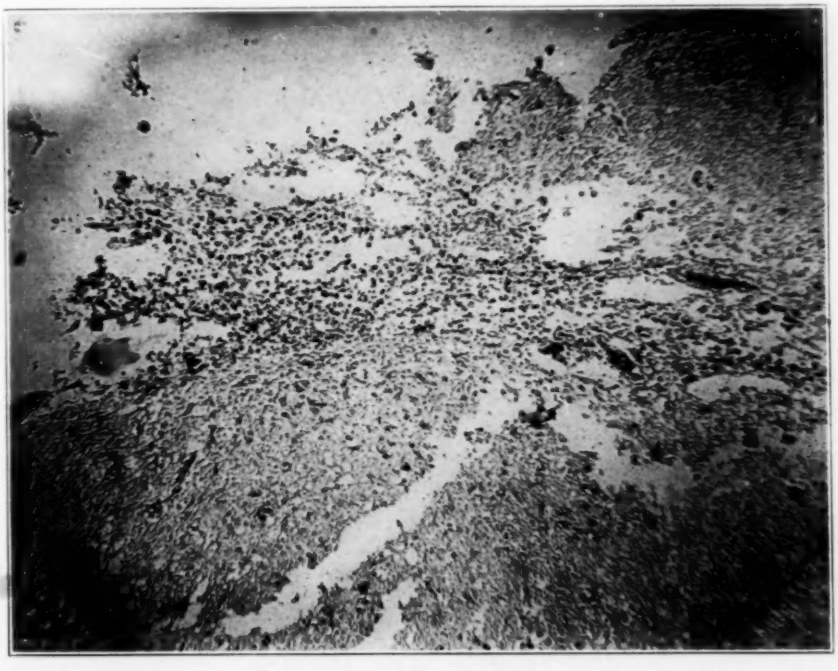


Fig. 11 (Case 2).—Canal near ventricle showing the amount of cellular detritus and phagocytic cells encountered in a canal at least seven months after injury.

est in the second case is the presence, on the ventricular surface overlying the wound canal, of a dense layer of well preserved red blood cells, seven months after the last injury. Rare giant cells were encountered in the vicinity of the older canals. Glial reaction was manifested by an increase of protoplasm. This reaction was more marked and more expansive in the cortical layers.

CONCLUSIONS

From the two cases studied, it appears that the brain is not damaged by injecting arsphenaminized serum into the ventricles except by the needle itself. At least, these cases show no more extensive damage than that reported in cases in which puncture was performed with sterile needles.

Observations in these cases are in keeping with previous reports that repair is accomplished by connective tissue elements.

HYPOPHYSIAL FAT DYSTROPHY WITH HYPERGLYCEMIA AND GLYCOSURIA

REPORT OF A CASE *

SHEPARD SHAPIRO, M.D.
AND
MARK G. KLIATSHCO, M.D.
NEW YORK

In 1901, Fröhlich [1] published a comprehensive description of the syndrome that bears his name. The disease is characterized chiefly by fat dystrophy and genital hypoplasia or atrophy, and results, it is believed, from insufficiency of the hypophysis. Probably all lobes of the gland are involved.

The adiposity is a constant accompaniment in all cases of the disease and manifests itself usually in a more or less marked deposition of fat in the thighs, hips and lower part of the abdomen, giving rise to the so-called "girdle obesity." The genital changes, however, may vary, depending on the time of life during which the process develops. If it occurs at or before puberty, there results arrested development of the gonads, libido sexualis does not appear, the patient is sterile, and the organs of generation remain in the infantile state. If the syndrome appears after maturity, one of several changes may be observed: The gonads may undergo no change discernible on physical examination, but the patient may show (and practically always does if the condition persists over a long period of time) a gradual failure of sex function. In the female, the menses become irregular and ultimately disappear. Frigidity is a prominent symptom. In the male, impotence almost always ensues. On the other hand, the glands of generation may all become strikingly atrophied. Such changes, of course, are accompanied by total loss of gonadal functions.

The metabolic changes have been considered an essential characteristic of the disease. There is usually a progressive increase in tolerance for carbohydrates. In some instances actual hypoglycemia has been observed. The occurrence of the excessive fat deposits is believed to result from this increased storage of glucose and subsequent conversion into fat. Similar phenomena are observed in other diseases in which there is likewise increased tolerance for carbohydrates, such as thyroid deficiency.

---

* From the Division of Laboratories and the Neurological Department of Montefiore Hospital, New York.

1. Fröhlich, A.: Ein Fall von Tumor der Hypophysis Cerebri ohne Akromegalie, Wien. klin. Rundschau **15**:883-906, 1901.

We have under observation at Montefiore Hospital a case of tumor in the region of the hypophysis, in which the patient presents, in addition to the typical picture of hypophysial fat dystrophy, not the supposed characteristic increase in carbohydrate tolerance but instead hyperglycemia, glycosuria and lowered sugar tolerance. Because of the presence of this unusual combination of symptoms, fat dystrophy progressing in spite of the apparent diabetes and a metabolic disturbance directly opposite in nature to that which is considered a fundamental characteristic of the disease, we are reporting the case.

REPORT OF CASE

History.—R. K., a woman, aged 32, a dressmaker, born in Poland, was admitted to Montefiore Hospital, Nov. 20, 1924, complaining chiefly of headaches, failing vision since 1918, general weakness and left-sided weakness since May, 1918, when a subtemporal decompression was performed. The family history was unimportant. The patient had been pregnant twice; with resultant miscarriage in February, 1920, and the birth of a monstrosity in June, 1924. The past history was essentially of no importance. Her greatest weight, 1923, was 182 pounds (82.6 kg.). She had been on a low caloric diet since November, 1924. Her weight on admission was 161 pounds (73 kg.), and at the onset of the illness in 1912 had been 125 pounds (56.7 kg.). Her menses began at 13, were of the twenty-eight day type and lasted three days. They were normal until 1912.

The present illness began in 1912, when the menses suddenly ceased. About the same time she commenced to have severe frontal and temporal headaches, which became almost constant. Concomitantly she noticed that her eyesight was failing, so that she soon became unable to read. In 1918 the menses began again. In May, 1918, a subtemporal decompression was performed; following this the patient had a left hemiplegia and became totally blind. The menses ceased again after the operation. In 1919, she began to regain her vision and menstruation reappeared, but this had been irregular since. Vision had shown no further change.

About February, 1920, the patient developed polyuria and polydypsia, at the same time gaining considerable weight with marked increase in subcutaneous fat. In 1923, she reached her maximum weight of 182 pounds (82.6 kg.). Since the onset of the illness she had become childish, and memory had become markedly impaired.

General Physical Examination.—The patient was an obese woman of rather low intelligence. Her skin was pink, clear and of delicate texture. The head was of average size, and well formed. There was a defect, about 4 by 2 cm. in size, in the right temporal region where decompression had been performed. Tension was not increased, and there was no fulness. The face was full and rounded. The ears, nose, mouth and throat presented no abnormalities. The neck was short and thick. The breasts were large and pendulous; the right breast showed a scar from an abscess that had been incised in February, 1922. The heart and lung findings were negative. The abdomen was very obese and full, so that palpation was impossible. The findings in the genitalia were negative; the cervix and uterus were small. There were no abnormalities in the extremities, except for a left hemiparesis.

Neurologic Examination.—The gait was that of a left hemiplegia with loss of normal associated movements of the left upper extremity. The mental reaction was characterized by a general sluggishness and slowness of response. There was a definite increase in the threshold of response. She was apprehensive about her condition, but there was a general lack of interest and slowness of cooperation. Memory was markedly impaired, more for recent than for past events. The patient executed simple arithmetical problems incorrectly. Her insight was good.

Smell was normal. Vision on the right was 20/50; left, 20/100; both fundi showed simple primary optic atrophy, more advanced in the left eye. There was slight left exophthalmos; the right palpebral fissure was slightly narrower than the left; both pupils were slightly irregular and unequal, the right being

Fig. 1.—Roentgenogram of skull showing sella turcica larger than normal and partial destruction of anterior and posterior clinoid processes.

larger than the left; there was a bilateral external rectus weakness. On upward gaze the left eye moved better and farther than the right; on downward gaze the right moved better than the left. The fifth nerve functioned normally. There was a left supranuclear weakness in the facial nerve. The auditory apparatus was normal, and there was no defect in the ninth, tenth, eleventh and twelfth nerves.

The right upper extremity was normal; the left showed markedly diminished power with spasticity. The reflexes were exaggerated, and there was a wrist clonus. The fourth and fifth were spread away from the other fingers. The upper left abdominal reflexes were not obtained. The right lower extremity

was normal; the left showed diminished power, spasticity, exaggerated tendon reflexes and a Babinski sign. On the left side of the body, except the face, light touch stimuli seemed rather unpleasant, and gave the impression of a nail scratch. There was definite hyperaffectivity in the responses. General cutaneous sensibility was impaired as compared with the right side. There was a fairly definite left astereognosis.

A roentgenogram of the skull showed an absence of an oval shaped area of bone about 6 by 4 cm. in the right temporal region. This was due to surgical removal of bone. The sella turcica was much larger than normal. There was partial destruction of the anterior and posterior clinoid processes. The entire picture was that of a hypophysial tumor.

Laboratory Findings.—Blood pressure readings were: 125 systolic, 82 diastolic; 120 systolic, 80 diastolic; 125 systolic, 80 diastolic. A blood count revealed: red cells, 3,500,000; hemoglobin, 75 per cent.; white cells, 6,240; polymorphonuclear cells, 65 per cent.; small lymphocytes, 18 per cent.; large lymphocytes, 10 per cent.; mononuclear cells, 4 per cent.; eosinophils, 2 per cent.; basophils, 1 per cent.

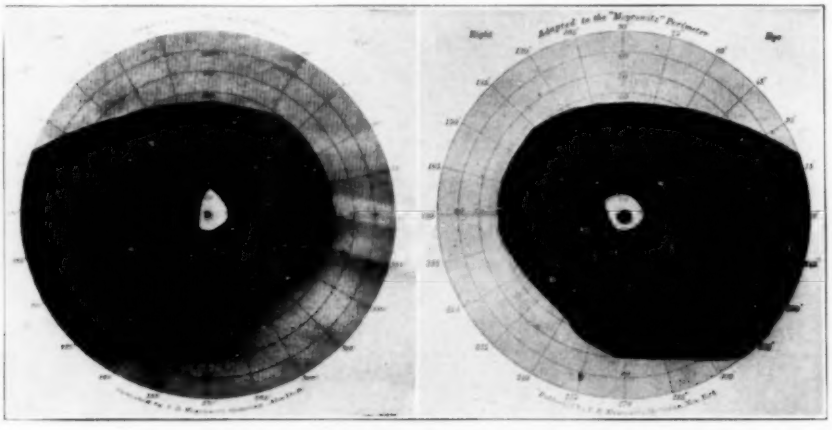


Fig. 2.—Contraction of the visual fields.

Urinalysis repeatedly showed glucose in varying amounts. On a diet containing protein, 75 gm.; fat, 150 gm., and carbohydrate, 50 gm., with a total value of 1,850 calories, the patient excreted from 3 to 5 gm. of glucose daily.

Findings of the urine concentration test were: at 8 a. m., 135 c.c. with a specific gravity of 1.006; at 9, 275 c.c. of 1.007; at 10, 56 c.c. of 1.015; at 11, 62 c.c. of 1.016; at 1 p. m., 260 c.c. of 1.006; at 3, 350 c.c. of 1.009; at 5, 53 c.c. of 1.020; at 7, 115 c.c. of 1.010; a total for twelve hours of 1.175 c.c. with an average specific gravity of 1.009.

The spinal fluid was clear and colorless, pressure normal. It contained no globulin; tests for sugar gave a normal reduction; the number of cells was 6 per cubic millimeter, and the Wassermann reaction was negative.

Blood chemistry revealed:

	Urea	Uric Acid	Sugar
10/31/24	15.4	4.8	420
11/24/24	15.3	3.7	262
3/11/25	35.0	3.5	210
5/ 8/25	18.9	3.1	169

Sugar tolerance test with 100 gm. of glucose given by mouth, May 13, 1925, revealed: first hour, 173; second hour, 272; third hour, 235; fourth hour, 215; fifth hour, 225.

Blood sugar and inorganic phosphate test, June 10, 1925, revealed: first hour, glucose, 173, phosphate, 3.6; second hour, glucose, 303, phosphate, 3.5; third hour, glucose, 313, phosphate, 3.4.

Blood Wassermann reaction was negative.

Basal Metabolism: The respiratory quotient was 0.86, the basal metabolism, minus 20 per cent.

SUMMARY

The diagnosis of pituitary tumor was made on the basis of: a history of amenorrhea and irregular menstruation, gain in weight, headaches and failing vision; the findings of girdle obesity, impaired mentality with slow cerebration, contracted visual fields and simple primary optic atrophy, and the roentgenogram showing a large sella with destruction of the posterior clinoids and floor. The motor and sensory findings in the left side of the body were sequelae of a right subtemporal decompression.

COMMENT AND CONCLUSIONS

Several questions arise: What is the nature of the diabetic condition presented by this patient? Is it pancreatic in origin, and are we dealing with a Fröhlich's syndrome with coincidental diabetes mellitus? Or, is the hyperglycemia and glycosuria similar in origin to that frequently observed in the developmental stage of acromegaly? From the laboratory data it appears that this patient reacted to carbohydrate in a manner similar to that of the ordinary diabetic patient, who is believed to be suffering from insular deficiency. However, clinically she presented none of the other symptoms common to this disease. There was no pronounced polyuria or nocturia; her appetite as regards sugars was normal; her skin was smooth and delicate. When placed on a diet of 2,000 calories or more she gained weight progressively. The presence of acetone bodies in the urine was never observed. Her blood inorganic phosphate curve was, according to Hartman and Bollinger,[2] that of a person with severe diabetes (which, obviously, clinically she was not), while the glucose tolerance curve was that of diabetes mellitus of moderate severity. Her basal metabolic rate was minus 20 per cent., the respiratory quotient was 0.86.

On the other hand, if the disturbance in glucose metabolism were due to an actual hypersecretion of the posterior hypophysial hormone, certain accompanying disturbances caused by an excess of pituitary secretion in the circulation should be present. We refer to changes in

2. Hartman, F. W., and Bollinger, A.: Blood Phosphates As Related to Carbohydrate Metabolism, J. Biol. Chem. **64**:91-109, 1925; J. A. M. A. **85**:653-656, 1925.

blood pressure and secretion of urine. Both of these were not abnormal. This speaks strongly against such hypersecretion.

It is claimed that in acromegaly when hyperglycemia and glycosuria are present they are caused by hypersecretion of posterior hypophysis hormone. The essential etiologic disturbance in acromegaly appears to be excessive function of the anterior lobe, which usually is adenomatous in this disease. The irritation of the secreting cells of the pituitary by this tumor is believed to cause excessive elaboration of posterior hypophysis hormone.

The patient described had a brain tumor located in the hypophysial region. This was definitely proved by both neurologic and roentgen-ray examinations. The possibility exists in this case, therefore, that, as in acromegaly, the irritation of the secreting cells of the pituitary by this neoplasm may cause such cells to over-function. However, regardless of what the etiology of the subnormal carbohydrate tolerance might be, in this case the important point is that a condition of fat dystrophy developed in the presence of this diabetic state. The infrequency of this phenomenon has been emphasized repeatedly in the literature. Kollarits,[3] in 1904, stated that glycosuria does not occur in tumors of the hypophysis without associated acromegaly. In fifty-two cases of hypophysial tumor without acromegaly, no patient had diabetes. Borchardt,[4] in 1908, likewise was unable to find any cases of neoplasm of the hypophysis without acromegaly that showed glycosuria. Frankl-Hochwart,[5] in 1909, reported a study of 155 cases of hypophysial fat dystrophy; two of them showed glycosuria. No details of these cases are given. Although a large number of clinical reports of adiposo-dystrophia genitalis are to be found in the French literature, urinalysis is rarely mentioned. However, in 1913, Sainton and Rol[6] asserted that although glycosuria may occur in pituitary tumor without acromegaly, nevertheless it is rare. Anders and Jameson[7] have found the frequency of "pituitary diabetes" without acromegaly to be as high as 35.7 per cent. (ten of twenty-eight cases). Recently Abrahamson[8] reported a case which he believes falls into this

3. Kollarits, J.: Hypophysistumoren ohne Akromegalie, Deutsch. Ztschr. f. Nervenk. **28**:85-105, 1904-1905.

4. Borchardt, L.: Die Hypophysenglykosurie und ihre Beziehung zum Diabetes bei der Akromegalie, Ztschr. f. klin. Med. **71**:332-348, 1908.

5. Frankl-Hochwart, L. von: Die Diagnostik der Hypophysentumoren ohne Akromegalie, Wien. med. Wchnschr. **59**:2127-2258-2326, 1909.

6. Sainton, P., and Rol, L.: Le diabéte hypophysaire, Gaz. d. hôp. **86**:1553-1557, 1913.

7. Anders, J. M., and Jameson, H. L.: The Relation of Glycosuria to Pituitary Disease and the Report of a Case with Statistics, Am. J. M. Sc. **148**: 323-329, 1914.

8. Abrahamson, L.: Fröhlich's Syndrome, Irish J. M. Sc., February, 1925, pp. 58-62.

category. The patient was a youth, aged 17, weighing 111 pounds (50 kg.) with infantile genitals and a blood pressure of 145 systolic and 90 diastolic. Roentgen-ray examination of the skull showed no sellar changes.

Apparently, therefore, the presence of diminished carbohydrate tolerance in hypophysial fat dystrophy is not common. On the contrary, in the majority of instances there is increased utilization of sugars, and it has been believed therefore that the fat dystrophy develops as a result of this augmented carbohydrate tolerance. Our contribution is offered as evidence that hypophysial fat dystrophy may develop even in the presence of an apparent diabetes mellitus. Consequently, we believe that, whatever the cause of Fröhlich's syndrome may be, the fat dystrophy is not necessarily dependent on an increased tolerance for carbohydrates.

ROENTGEN-RAY TREATMENT OF PITUITARY TUMORS *

E. B. TOWNE, M.D.
SAN FRANCISCO

Patients suffering from pituitary tumors usually apply for relief of loss of vision, caused by pressure on the optic nerves or tracts. In this country, treatment has been almost entirely surgical. For several years there have been reports, especially in the French literature, of results following roentgen-ray treatment which compare favorably with those of surgery. I report here on two patients, who, after periods of more than three and two years, respectively, of roentgen-ray treatment,[1] remain free from the effects of intracranial extension of pituitary adenomas. I [2] have reported another suspected pituitary tumor which was treated with the roentgen ray. These three cured cases represent my entire experience with this method.

CASE REPORTS

CASE 1 (Newell's [3] Case 7571).—*Intracranial extension of pituitary adenoma, causing loss of visual acuity, constriction of visual fields, and partial external ophthalmoplegia. Cure following roentgen-ray treatment; no recurrence after three and one-fourth years. Decrease in size of tumor demonstrated by movement of areas of calcification in roentgenograms.*

History.—L. L., a woman, aged 45, married, a storekeeper, seen in January, 1922, complained of loss of vision, double vision, headache, vomiting, nervousness and weakness. She bore two children before she was 20 years old. Her menstrual periods stopped, without operative interference, when she was 24 years old. For twenty years she had suffered from attacks of bitemporal headache, nausea and vomiting, which lasted two or three days of each week. Vision had failed for two years, and she had not been able to read or sew for eight months. Double vision had been present for five months. She stopped work eight months before admission.

Examination.—The patient was pale and poorly nourished, weighing 89 pounds (40.4 kg.). Her mental processes were slow. The right pupil reacted

---

* From the Department of Surgery, Stanford University Medical School.

* Results of roentgen-ray treatment of other intracranial tumors have been reported: Towne, E. B.: Roentgen-Ray Treatment of Tumors of the Brain, J. A. M. A. **84**:1813 (June 13) 1925.

1. Both patients were treated at Stanford University Hospital by Dr. W. E. Chamberlain and Dr. R. R. Newell.

2. Towne, E. B.: Cessation of Diabetes Insipidus on Roentgen-Ray Treatment of Pituitary Gland, J. A. M. A. **83**:2085 (Dec. 27) 1924.

3. Newell, R. R.: Calcification in Brain Tumors, S. Clin. N. Amer. **3**:775 (June) 1923.

sharply to light, and outward motion of the eyeball was defective—a sixth nerve paresis. The left pupil was larger than the right, and reacted sluggishly to light; the left lid drooped, and inward, upward and downward motions of the eyeball were defective—a third nerve paresis. The optic disks were pale, and the retinal arteries were slightly diminished in caliber. Visual acuity in the right eye was 15/70, and in the left, ability to count fingers at a distance of 1 meter. The visual fields showed, on the left, loss of central vision, loss of the upper quadrant of the temporal field and partial loss of the lower quadrant of the temporal field; on the right, a relative central scotoma and partial loss of the lower quadrant of the temporal field (Fig. 1). There was a pathologic great toe reflex on the right. Roentgenograms of the skull showed destruction of the floor and dorsum of the sella, erosion of the left anterior clinoid process, and three spots of calcification near the midline—one posterior to the anterior clinoid processes, one in about the normal location of the pineal

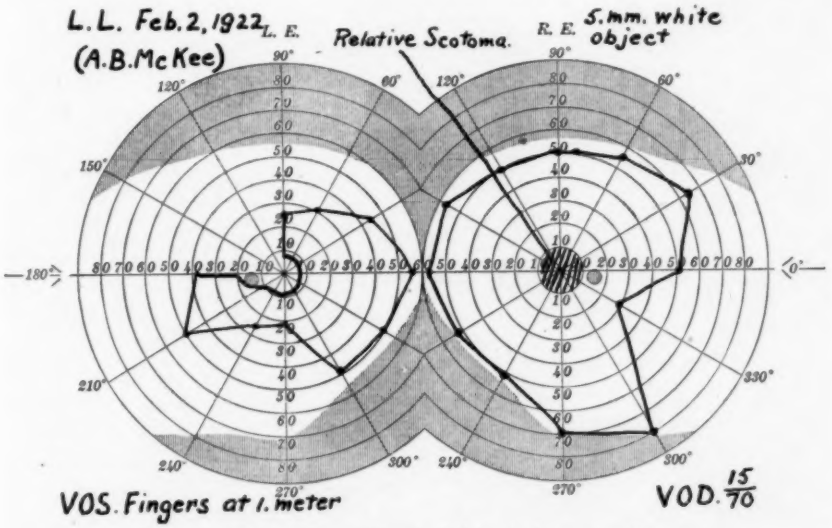


Fig. 1 (Case 1).—Visual fields before treatment.

gland and one above and posterior to the second (Figs. 2 and 5, *A*). Besides these findings, visceral and neurologic examination and laboratory tests were negative.

Diagnosis.—Three possibilities were considered: (1) an adenoma with a large intracranial extension showing three areas of calcification; (2) a pharyngeal pouch or suprasellar tumor, eroding the sella secondarily; (3) two lesions; a pineal tumor outlined by the two upper calcifications and a pituitary adenoma with intracranial extension visualized by the lower calcification. The diagnosis of anterior lobe adenoma seemed the most probable, because of the early amenorrhea, and because the changes in the sella were characteristic of an intrasellar tumor. Unless the possibility of two tumors was to be seriously considered, this diagnosis forced the conclusion that the three spots of calcification were in an enormous intracranial extension of the tumor.

Treatment.—Surgery seemed to be contraindicated by the patient's poor general condition, especially as the size of the tumor would require approach under the frontal lobe, with its high operative mortality. Roentgen-ray treat-

ment was therefore started. On February 6, a dose of 50 milliamperes, at 12-inch distance, with 10-inch spark, and 5 mm. aluminum filter, was applied to a skin area of 3 inches (7.6 cm.) square in each temporal region. This was approximately one third of a maximum skin dose. On February 7, the same dose was applied to three areas over the forehead, vertex and occiput. Similar treatments were given once a month from that time until the present (June, 1925); except that, after seven treatments, the vertex area was abandoned because of epilation.

Result.—The eye muscle palsies began to clear up after the first treatment, but diplopia did not entirely disappear until August, 1922. Vomiting ceased after the second series. The patient returned to work in April, 1922. She had

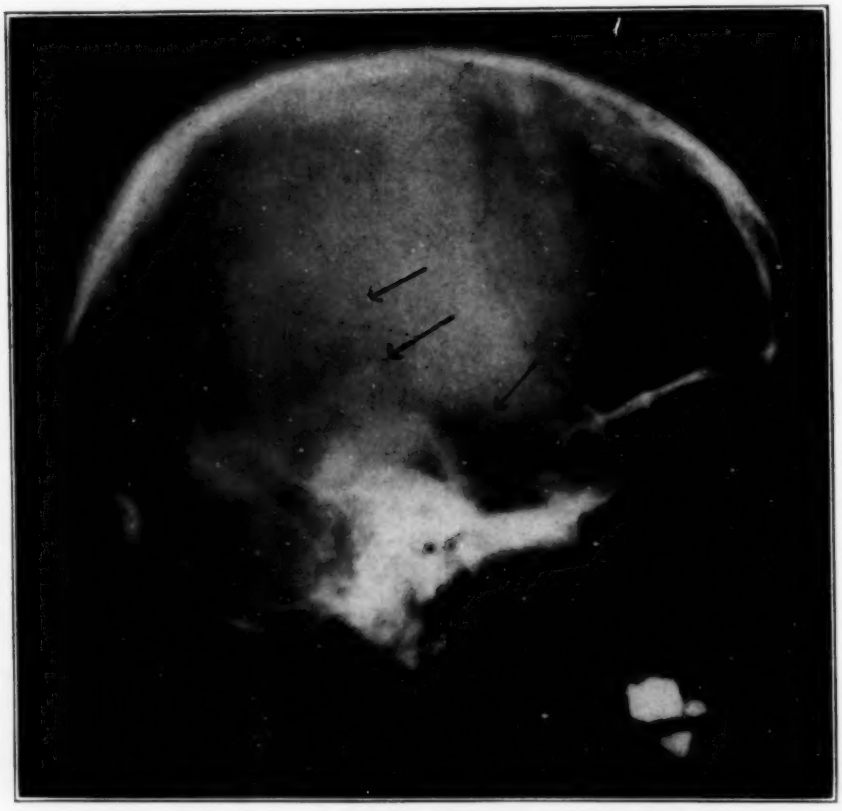


Fig. 2 (Case 1).—Destruction of floor and dorsum of sella and three areas of intracranial calcification. (Compare with Fig. 5.)

no more headaches after the fourth series of treatments. Visual acuity improved gradually. She could read large type in June, 1922; but no accurate measurements were made until March, 1923, when visual acuity in the right eye was 20/50, and in the left, 20/30. The visual fields had widened, as shown in Figure 3. The next perimetric measurements were made in August, 1924, and they showed normal visual fields and 15/20 visual acuity in each eye (Fig. 4).

Tracings of roentgenograms of the skull made in August, 1924, and of those made in February, 1922, corrected for magnification, showed that the areas of

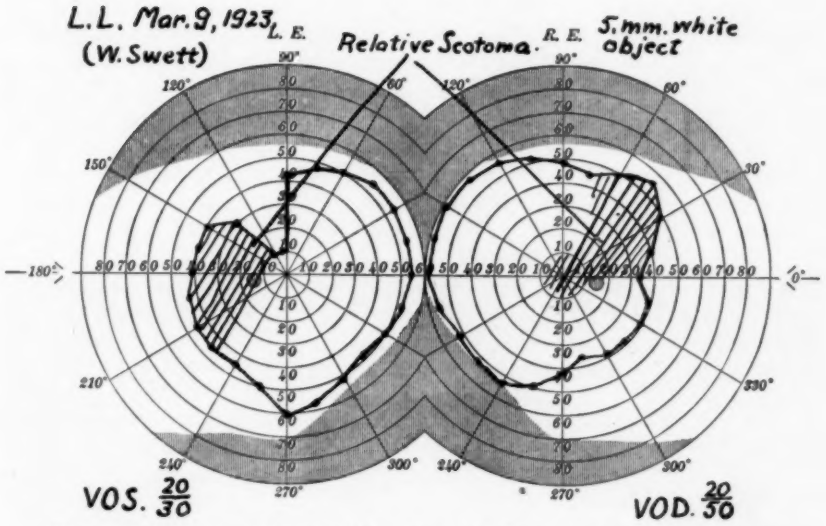


Fig. 3 (Case 1).—Visual fields after thirteen months of treatment.

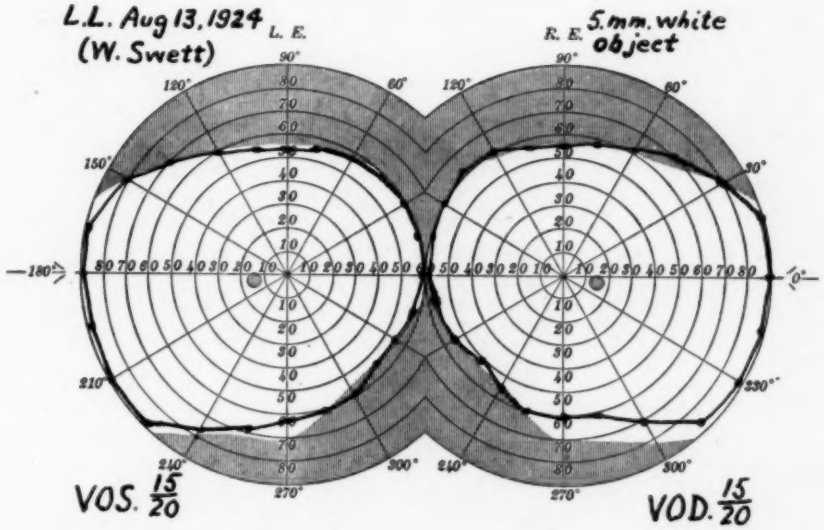
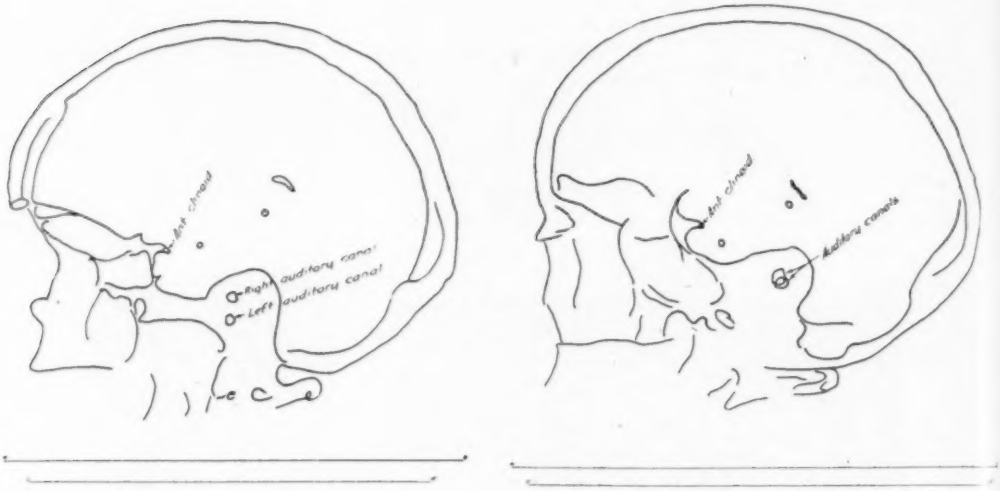


Fig. 4 (Case 1).—Visual fields after two and a half years of treatment.



5 A 5 B

Fig. 5 (Case 1).—*A*, tracing of roentgenogram of February, 1922 (compare with Fig. 2); *B*, tracing of roentgenogram of August, 1924, to show downward and forward displacement of calcifications after two and a half years of treatment.

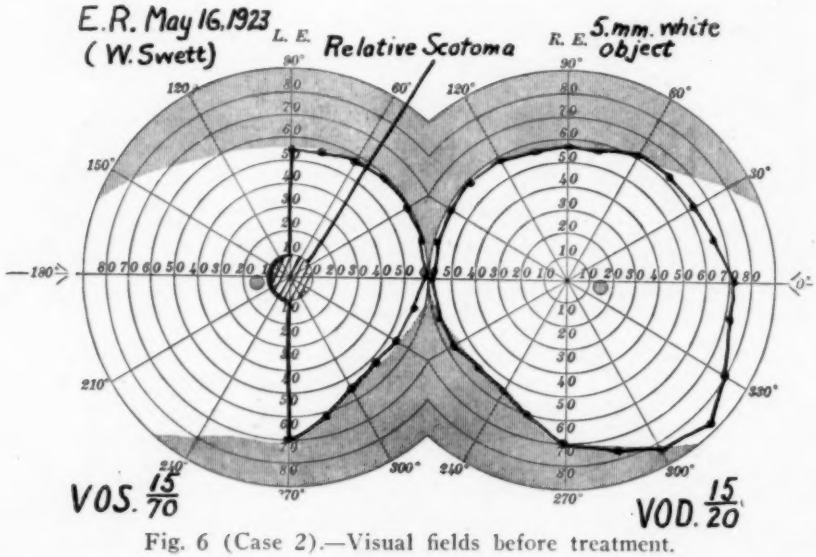


Fig. 6 (Case 2).—Visual fields before treatment.

calcification had moved downward and forward during that period of two and a half years, the lower and middle spots about 1 cm., and the upper more than 1.5 cm. (Fig. 5).

Perimetric examinations made in January and May, 1925, showed normal visual fields and 20/20 visual acuity in each eye. In January, 1925, the patient was working eight or nine hours a day. In May, 1925, she weighed 103 pounds (46.7 kg.); her general physical condition was excellent, and she was very alert mentally.

CASE 2.—*Intracranial extension of pituitary adenoma causing loss of visual acuity and constriction of visual field of left eye. Cure following roentgen-ray treatment; no recurrence after two years.*

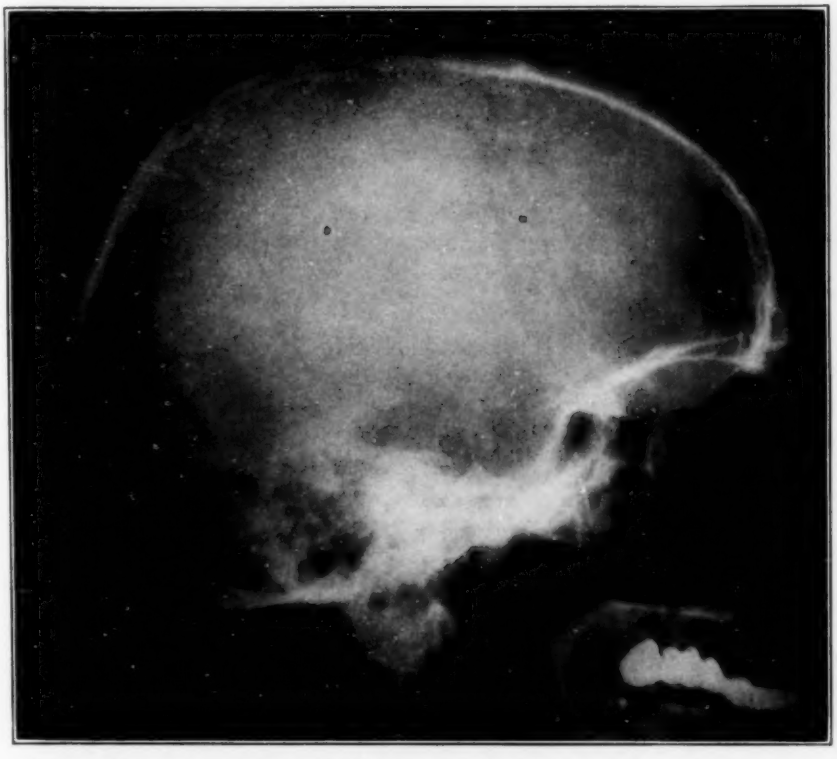


Fig. 7 (Case 2).—Enlarged sella; corrected measurements; vertical 16 mm., horizontal 18 mm.

History.—E. R., a man, aged 42, married, a watchmaker, seen in May, 1923, complained of loss of vision for two months. He had been married twelve years, and his wife had not been pregnant. Sexual appetite and power had been lost for two years. Eight weeks before admission, he was not able to do his work with the right eye, and, on trying the left eye, he found that it was worse than the right. With the right eye closed, he could see only a part of objects with the left eye. He had not had headaches, but for several months he had noticed a feeling of fullness above the eyes, which had been temporarily relieved by severe nosebleeds. For three months he had been very drowsy. His usual weight of 165 pounds (74.8 kg.) had not changed.

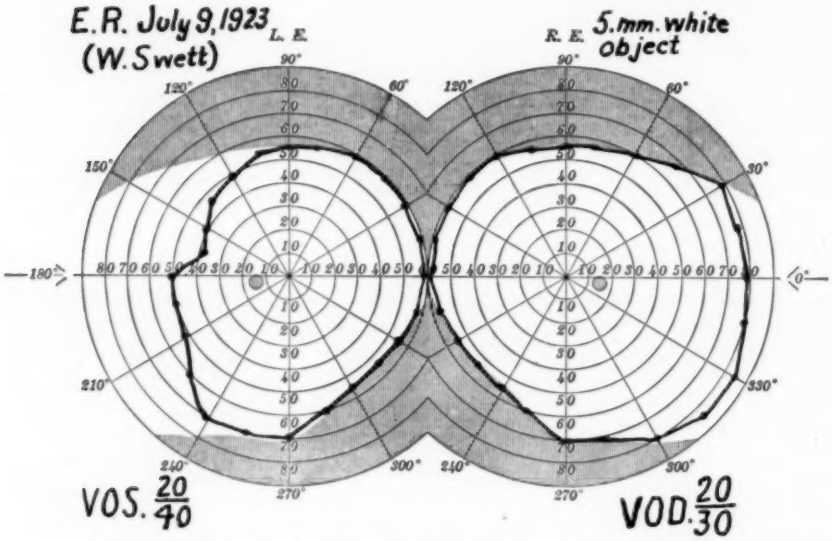


Fig. 8 (Case 2).—Visual fields after two series of treatment.

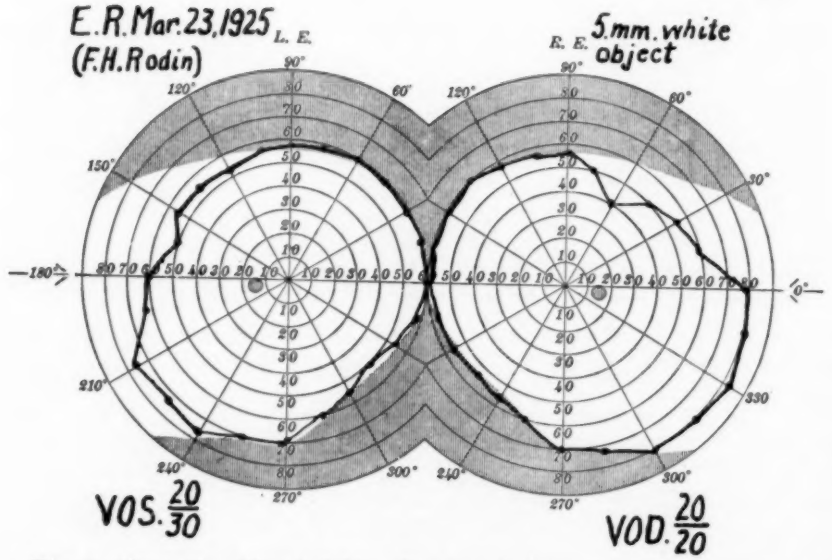


Fig. 9 (Case 2).—Visual fields after twenty-two months of treatment.

Examination.—The patient was an obese man with a dull, sleepy countenance. He answered questions slowly. The beard and axillary hair were scanty, and the distribution of pubic hair was of the feminine type. The skeletal development was not abnormal. The testes were not atrophic. Visual acuity was 15/20 in the right eye and 15/70 in the left. Perimetric examination showed blindness of the temporal field of the left eye (Fig. 6). The left optic disk was slightly paler than the right. Roentgenograms of the skull showed an enlarged sella, with corrected measurements of 18 mm. from before backward, and 16 mm. from above downward (Fig. 7).

Diagnosis.—The enlarged sella and the constricted visual field indicated a pituitary adenoma with intracranial extension.

Treatment.—There was no contraindication to surgical treatment; but, in view of the result in the first case, it seemed desirable to test the effect of the roentgen ray. One third of a maximum skin dose was given once a month from May, 1923, until the present time (June, 1925). After ten months the frontal and occipital areas were omitted, and he was treated over only three areas each time.

Result.—In July, 1923, there was a considerable return of the left visual field, and visual acuity in the left eye had increased to 20/40 (Fig. 8). Perimetric examinations at intervals of two or three months showed gradual improvement in the left visual field. After April, 1924, visual acuity in the left eye was 20/30, and in March, 1925, visual acuity in the right eye was 20/20. The chart of March, 1925, is shown in Figure 9. The patient was able to carry on his work after July, 1923. He became much more active and alert. Potentio sexualis did not return.

COMMENT

No satisfactory comparison between surgical and roentgen-ray treatment of pituitary tumors can be made as yet. There are large and carefully studied series of cases treated by operation, of which the most notable is that of Cushing,[4] based on 189 verified tumors. On the other hand, there are numerous reports of a few cases of pituitary tumor treated with roentgen ray, some adequately studied, some lacking important details, and almost all, necessarily, histologically unverified. However, recognizing the limitations of the material on roentgen-ray treatment, I will attempt to draw some conclusions on the scope, danger and results of the two methods.

Scope.—The more common pituitary tumor is the anterior lobe adenoma, which is primarily an intrasellar growth. Cushing reported 154 cases of adenoma and thirty-five cases of the less common lesion, the pharyngeal pouch tumor, which is usually primarily a suprasellar growth. The adenomas cause changes in the sella which can be detected in the roentgenogram, and do not cause visual disturbances until they have broken through the diaphragm of the sella and extended well into the cranial cavity. Pharyngeal pouch tumors cause loss of vision by

4. Cushing, Harvey: Les syndromes hypophysaires au point de vue chirurgical, Rev. neurol. **38**:779 (June) 1922.

pressing on the optic tracts, and change the contours of the sella only at a late stage, if at all, by eroding the clinoid processes. They are usually cystic, and frequently contain areas of calcification which show in the roentgenogram. These tumors do not respond favorably to the roentgen ray, probably because they are cystic. Some adenomas are also cystic (twenty-seven in Cushing's series of 154), and it may be assumed that they also will not be influenced by the roentgen ray. The field for roentgen-ray treatment is therefore limited to solid adenomas of the anterior lobe. As the diagnosis between solid and cystic adenomas is impossible, failure of an intrasellar tumor to respond to roentgen-ray treatment would suggest that the adenoma was cystic, and required operative treatment.

Danger.—Cushing's statistics give the lowest mortality which has been attained in a large series of surgically treated cases. In 151 primary transsphenoidal operations, with partial extirpation of an adenoma, there was an operative mortality of 7.9 per cent. There will be little information on the mortality of roentgen-ray therapy until larger series of consecutive cases are reported. Béclère,[5] who has had a large experience, called roentgenotherapy "a method of treatment free from danger." Bailey[6] reported on a patient (C. C., T. 631) who, a few hours after a roentgen-ray treatment, developed rapid and marked loss of vision, which persisted until after partial transsphenoidal removal of an edematous and necrotic tumor. It should be noted that Bailey's patients who had pituitary disease were given a maximum skin dose, and that my patients were given one third of a maximum skin dose.

Early and Late Results.—Cushing's figures on early results, based on 151 primary transsphenoidal operations with partial extirpation of the tumor, showed marked improvement of visual acuity and fields in seventy-eight cases (52 per cent.), some improvement in twenty-seven cases (18 per cent.), and no change in thirty-four cases (22.5 per cent.). He said, "It is rather more difficult to give an exact idea of the duration of the improvement . . . even when the improvement has been definite and the vision has been regained, there has been usually some degree of recurrence after a period of about two years." Cushing performed 243 operations on 189 patients, and he remarked, "The fact that the number of operations much exceeds the number of patients proves that subsequent operations have been undertaken when the first failed in its object, or when, the first operation having caused improve-

5. Béclère, A.: Technique, résultats, indications et contre-indications de la roentgenthérapie des tumeurs hypophysaires, Rev. neurol. **38**:808 (June) 1922.

6. Bailey, Percival: The Results of Roentgen Therapy on Brain Tumors, Am. J. Roentgenol. **13**:48 (Jan.) 1925.

ment, there has been a recurrence of symptoms." However, thirty-nine of his patients conserved useful vision for more than five years after a transsphenoidal operation.

There are numerous reports of cases in which the visual acuity and fields improved to a greater or less degree after roentgen-ray treatment. I have found only one case, that of Carlotti,[7] in which, following roentgen-ray treatment, there was complete cure of a condition comparable to that of my first patient. There are reports of cases which showed no improvement following roentgen-ray treatment; in some of these the diagnosis of tumor is open to question, and in others, the tumor was suprasellar, as shown by a normal sella in the roentgenogram.

The late results of roentgen-ray treatment appear to be at least as good as those of surgery. My first patient has been under treatment only three and one-fourth years without a recurrence of symptoms; but the duration in Carlotti's case was more than six years, and in one of Béclère's cases, thirteen years. Froment [8] referred to other cases in which the amelioration had lasted for four or more years. Bailey [6] reported an illuminating case from Cushing's clinic. A woman (Surg. No. 12494) had failing vision and signs of a pituitary tumor. In July, 1920, an adenoma was partly removed by the transsphenoidal route. Fifteen months later there was a recurrence of symptoms, and the tumor was again partly removed by the transfrontal route. After the second operation, roentgen-ray treatment caused "definite improvement following these treatments, and failure of vision during periods of nontreatment, as shown by repeated examination of the visual fields." Visual acuity of the right eye improved from 20/200, after operation, to 20/40 in August, 1923. This is the only recorded case which proves that the roentgen ray may give lasting results after surgery has failed to do so.

SUMMARY AND CONCLUSIONS

Two types of pituitary neoplasm cause loss of visual acuity and constriction of the visual fields by pressing on the optic tracts. The less common pharyngeal pouch tumor is primarily suprasellar and usually cystic. It is not favorably influenced by roentgen-ray treatment, and remains a surgical problem. The more common anterior lobe adenoma, primarily intrasellar, enlarges and erodes the sella, and later invades the cranial cavity and causes visual disturbances. This tumor is usually diagnosed without difficulty by means of the roentgenogram and the perimeter. About 20 per cent. of the adenomas are cystic. Many of these tumors respond to roentgen-ray treatment with increase of visual

7. Carlotti: Tumeurs de l'hypophyse et troubles visuels. Symptomes, radiothérapie, Ann. d'Oculistique **159**:1 (Jan.) 1922; obs. 1.

8. Froment, J.: Rev. neurol. **38**:649 (June) 1922.

acuity and enlargement of visual fields, even to normal. If an adenoma is not favorably influenced by the roentgen ray, one may suspect cystic degeneration which calls for surgical treatment.

Two cases are reported in which the visual fields and visual acuity returned to normal following cross-fire treatment with one third of a maximum skin dose of roentgen ray once a month. No recurrence has taken place up to the present time, three and one-fourth and two years after the treatments were started. In the first case, a partial external ophthalmoplegia disappeared promptly, and measurable decrease in the size of the large intracranial extension of the tumor was demonstrated by shifting of areas of calcification in roentgenograms taken before, and two and a half years after, the institution of treatment.

All adenomas of the pituitary gland should be treated with moderate doses of roentgen ray, and progress should be followed by repeated perimetric examinations. Operation should be undertaken only if visual acuity and the fields do not improve. There is good reason to believe that when roentgen-ray treatment gives a favorable result the risk is less and the result more lasting than that of surgical treatment.

Stanford University Hospital.

THE AMYOSTATIC SYNDROME OF EPIDEMIC ENCEPHALITIS

BLOOD SUGAR TOLERANCE STUDIES *

THEOPHILE RAPHAEL, M.D.
OLIVE M. SEARLE, M.S.
AND
WILLIAM G. FERGUSON, M.D.
ANN ARBOR, MICH.

The obvious clinical resemblance between certain aspects of the amyostatic syndrome of epidemic encephalitis and certain manifestations in schizophrenia, particularly of the so termed catatonic order, has been remarked by numerous observers (Bostroem,[1] Deny and Klippel [2] and others). This raises in a general way the question of the possibility of the occurrence, in some respects, in both disorders, of a somewhat similar pathology. Furthermore, it has been actually determined through study along more or less strictly histopathologic lines that in schizophrenia, among other attributes, there does seem to obtain a pathology of like locale to that in epidemic encephalitis. In this connection reference is made especially to the work of Laignel-Lavastine,[3] Marcuse,[4] Fünfgeld,[5] Reichardt,[6] Josephy,[7] Buscaino [8] and Freeman.[9] Jelliffe's [10] comment in this connection is especially interesting:

---

* From the State Psychopathic Hospital, Ann Arbor, Mich.

1. Bostroem, A.: Encephalitische u. katatonische Motilitätsstörungen, Klin. Wchnschr. **3**:465 (March) 1924.

2. Deny, G., and Klippel, M.: Epidemic Encephalitis with the Semblance of Dementia Praecox, Rev. neurol. **29**:402 (April) 1922.

3. Laignel-Lavastine et al.: Lesions of the Corpus Striatum in the Catatonic Form of Dementia Praecox, L'Encephale **17**:151, 1922.

4. Marcuse, H.: Doppelkernige Thalamuszellen bei Schizophrenie, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:777 (April) 1925.

5. Fünfgeld, E.: Ueber anatomische Untersuchungen bei Dementia Praecox mit Berucksichtigung des Thalamus Opticus, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:411 (March) 1925.

6. Reichardt, cited by Jelliffe: Tr. Assn. Res. in Nerv. & Ment. Dis. **3**:83, 1925.

7. Josephy, cited by Jelliffe, Footnote 6.

8. Buscaino, V. M.: Review of Findings in the Pathological Anatomy of the Nervous System in Dementia Praecox, Riv. di patol. nerv. **26**:57 and 87, 1921.

9. Freeman, W. J.: Lipoid Degeneration Products in the Thalamus and Globus Pallidum of Schizophrenia, to be reported at the December, 1925, meeting of the Association for Research in Nervous and Mental Diseases, New York.

10. Jelliffe, S. E.: The Parts of the Central Nervous System Which Tend to Exhibit Morbid Recessive or Dominant Characters, Tr. Assn. Res. in Nerv. & Ment. Dis. **3**:83, 1922.

No analysis of the dementia praecox situation is availing which leaves out of consideration the so-called motor phenomena, the catatonic, cataleptic, motor stiffness, loss of spontaneity, perseveratory activities in automatic motions, speech automatisms, etc. Such myostatic disturbances are rightly referred to striatal disturbances and their so-called physical correlates are striking, particularly in the defenses set up against paying attention to incoming stimuli because of inefficient symbolic delivery.

In view of this and the notable obscurity still prevailing with respect to the general concept of schizophrenia, especially its possible structural or organic aspect, it was felt that it might prove of a certain interest to study, in the late amyostasis of epidemic encephalitis, the nature of the blood sugar tolerance response. This reaction has been examined in schizophrenia [11] in the acute cases of which, particularly those of catatonic type, a rather characteristic curve form (Chart 1, *A*) is obtained. This is essentially a curve of delayed tolerance with evidence of an initial relative hypoglycemia. Of definite significance in this relation is the noting of a similar type of blood

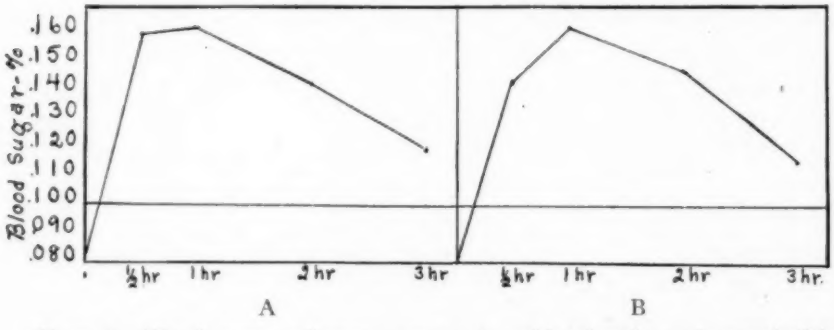


Chart 1.—Blood sugar tolerance curves in schizophrenia and encephalitis. *A*, indicates the blood sugar tolerance (average) in eight unselected cases of acute schizophrenia, *B*, blood sugar tolerance (average of Chart 3 A) in eight unselected cases of encephalitis with severe to moderate amyostasis.

sugar response in a series of cases presenting noninfectious striate disorder,[12] to which we have added another from our own service, including, in all, three cases of Huntington's chorea—two of paralysis agitans and one of congenital double athetosis (Chart 2).

For the present study there were utilized fifteen cases of late epidemic encephalitis, all presenting definitely, although in varying degree, the typical picture of the amyostatic syndrome (Table 1), afebrile

11. Raphael, T., and Parsons, J. P.: Blood Sugar Studies in Dementia Praecox and Manic Depressive Insanity, Arch. Neurol. & Psychiat. **5**:687 (June) 1921. Raphael, T.: The Physiologic Level in Dementia Praecox, Am. J. Psychiat. **2**:515 (April) 1923.

12. Raphael, T., and Potter, F. C.: Blood Creatinin Findings in Five Cases of Corpus Striatum Disorder, J. Nerv. & Ment. Dis. **55**:492 (June) 1922.

and free, so far as could be clinically determined, from other pathologic disturbance which might operate of itself to affect the tolerance reaction.

The procedure followed with reference to glucose administration was that outlined by Janney and Isaacson,[13] and the actual blood sugar determinations were carried out according to the technic of Folin and Wu.[14]

TABLE 1.—*Encephalitic Cases Utilized*

Cases	Age	Sex	Status	Duration, Years
1. A.	29	M	Moderate to severe amyostasis	1½
2. D.	34	M	Moderate to severe amyostasis	4
3. Ha.	24	M	Moderate to severe amyostasis	1½
4. Hu.	42	F	Moderate to severe amyostasis	5
5. Mak.	28	F	Moderate to severe amyostasis	4
6. Maj.	35	F	Moderate to severe amyostasis	2
7. McD.	25	M	Moderate to severe amyostasis	6
8. S.	28	F	Moderate to severe amyostasis	5
9. Had.	26	M	Severe amyostasis with marked motor agitation	5
10. Mi.	33	F	Severe amyostasis with marked motor agitation	2
11. F.	34	M	Mild amyostasis	1
12. McC.	22	F	Mild amyostasis	5
13. Mit.	20	M	Mild amyostasis	1½
14. N.	28	M	Mild amyostasis	2½
15. W.	19	M	Mild amyostasis	1

TABLE 2.—*Blood Sugar Determinations in Encephalitic Cases*

Cases	Blood Sugar Percentage				
	Fasting	½ Hour	1 Hour	2 Hours	3 Hours
Severe amyostasis					
1. A.	0.088	0.149	0.175	0.128	0.126
2. D.	0.075	0.160	0.211	0.174	0.074
3. Ha.	0.077	0.130	0.131	0.105	0.072
4. Hu.	0.072	0.160	0.203	0.200	0.166
5. Mak.	0.087	0.149	0.168	0.167	0.158
6. Maj.	0.086	0.172	0.160	0.154	0.111
7. McD.	0.083	0.104	0.125	0.118	0.093
8. S.	0.091	0.132	0.131	0.138	0.133
Severe amyostasis with marked motor agitation					
9. Had.	0.077	0.167	0.185	0.054	0.072
10. Mi.	0.080	0.177	0.124	0.097	0.071
Mild amyostasis					
11. F.	0.098	0.152	0.159	0.100	0.060
12. McC.	0.085	0.117	0.133	0.094	0.077
13. Mit.	0.091	0.174	0.140	0.100	0.087
14. N.	0.076	0.101	0.089	0.089	0.072
15. W.	0.089	0.123	0.100	0.111	0.080

The results determined (Table 2 and Charts 3 and 1, *B*) indicate, on the whole, a definite deviation from the accepted average normal curve (Chart 4, *A*) and a striking resemblance to the general type of curve form determined in schizophrenia (compare Chart 1), particularly as regards the relatively low initial sugar level and the obviously

13. Janney, N. W., and Isaacson, V. I.: A Blood Sugar Tolerance Test, J. A. M. A. **70**:1131 (April 20) 1918.

14. Folin, O., and Wu, H.: A System of Blood Analysis, Supplement I. A Simplified and Improved Method for Determination of Sugar, J. Biol. Chem. **41**:367 (March) 1920.

delayed return to the starting base line within the standard two-hour period. If one may accept the feeling of numerous recent workers (Foster,[15] Graham,[16] John [17] and Drury [18]) that this critical time period for return to the initial starting level should be shorter than two hours, one and a half hours at the most, the abnormality apparent in these cases is of even greater extent (Chart 4, *B*).

It is of no little interest to note, as shown on the charts, that this deviation in sugar tolerance reaction was manifested most strikingly (Chart 3, *A*) where the objective disturbance was of moderate to severe degree, and definitely less so where the objective syndrome was relatively

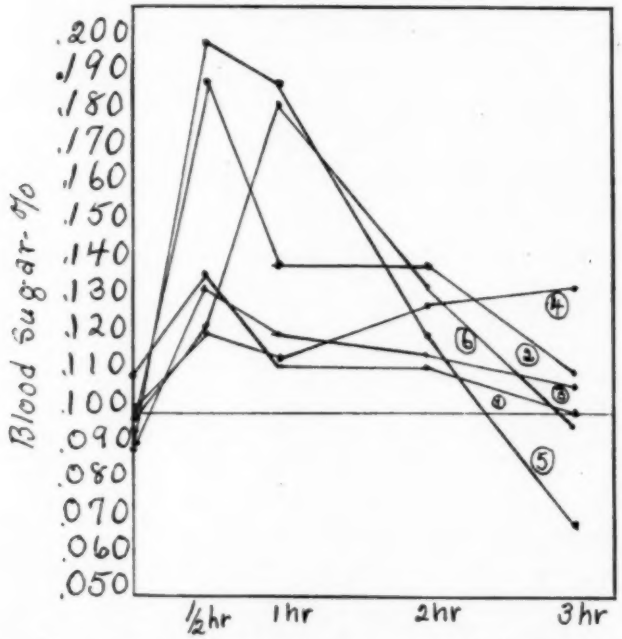


Chart 2.—Blood sugar tolerance curves in noninfectious striatal disorder. 1. Indicates Huntington's chorea; 2, Huntington's chorea; 3, Huntington's chorea; 4, paralysis agitans; 5, paralysis agitans; 6, congenital double athetosis.

15. Foster, G. L.: Studies in Carbohydrate Metabolism I. Some Comparisons of Blood Sugar Concentrations in Venous and Finger Blood, J. Biol. Chem. **55**:291 (Feb.) 1923.

16. Graham, G.: Variations in Blood Sugar in Health, J. Physiol. **50**:285 (July) 1916.

17. John, H. J.: Glucose Tolerance and Its Value in Diagnosis, J. Metab. Res. **4**:256 (Sept.-Oct.) 1923.

18. Drury, K. K., et al.: Observations on the Types of Blood Sugar Curve Found in Different Forms of Insanity, J. Ment. Sc. **71**:8 (Jan.) 1925.

mild (Chart 3, *C*). This same general relationship between clinical acuity and sugar response has been determined in schizophrenia also (Raphael [11]).

Two cases (Chart 3, *B*), in which there was severe amyostasis and which in addition evidenced tremendous and continuous motor agitation and tremor, on the whole showed similar curves, particularly as regards low initial sugar level, but with definitely lesser delay in base line return, apparently depending directly on the effect of the muscular activity. This fitted in very well with observations made by Gordon and his associates on Marathon runners.[19]

Affording a certain corroboration to the findings in the present study is the work of Halliday,[20] who reports blood sugar determinations in association with his examination of the spinal fluid sugar content in

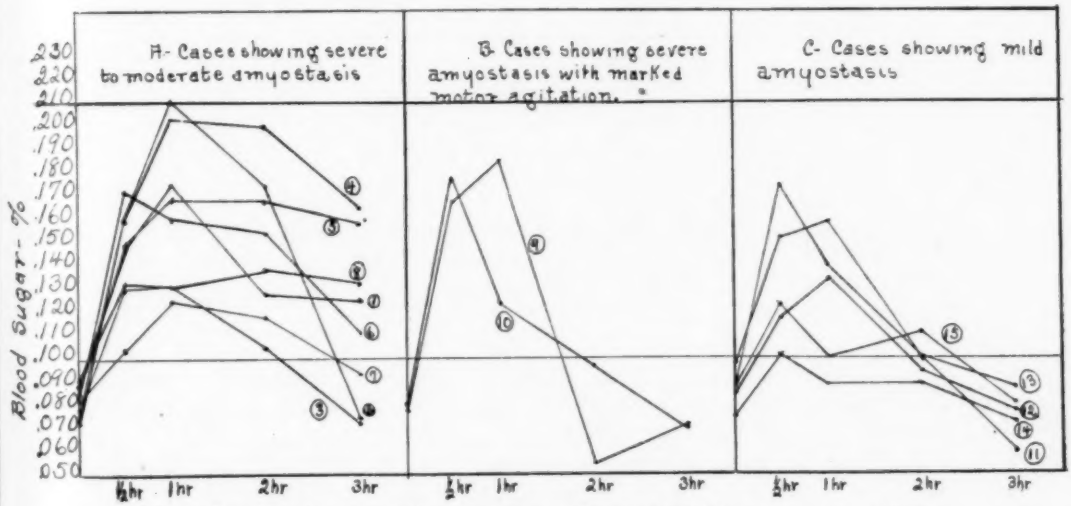


Chart 3.—Blood sugar tolerance curves in encephalitic cases. *A* indicates cases showing severe to moderate amyostasis; *B*, cases showing severe amyostasis with marked motor agitation; *C*, cases showing mild amyostasis.

epidemic encephalitis. However, Halliday's cases were all acute and febrile, thus introducing a complicating toxic factor, which, it has been found, may affect sugar tolerance.[21] Halliday further employed the MacLean technic for blood analysis, originally a micro-method, for

19. Gordon, B., et al.: Sugar Content in the Blood in Runners Following a Marathon Race, J. A. M. A. **85**:508 (Aug.) 1925.

20. Halliday, J. L.: The Spinal Fluid Sugar in Encephalitis, Quart. J. Med. **18**:300 (April) 1925.

21. Gordon, B., in Footnote 19. Olmsted, W. H., and Gay, L. P.: Study of Blood Sugar Curves Following a Standardized Glucose Meal, Arch. Int. Med. **29**:384, 1922.

which presumably capillary blood is utilized, which returns higher values than venous blood with more prolonged elevation above the base line. In Halliday's cases also, from the standpoint of sugar administration, an arbitrary amount—50 gm.—was given to each patient, a procedure which is not regarded as quite as satisfactory, particularly from the standpoint of specific tissue absorption,[22] as the regulating of the sugar dosage to body weight as is the case with the Janney-Isaacson method. Suggestive in this regard also is the report of Schwab,[23] utilizing the Myers-Bailey and Hartman-Schaffer sugar technics, of seven encephalitic cases in association with a number of other neurologic and psychiatric types. These cases, although presented without comment, particularly as to phase or status, showed in the majority indication of delay in blood sugar tolerance, mild to severe in degree, in keeping with results determined in our own study.

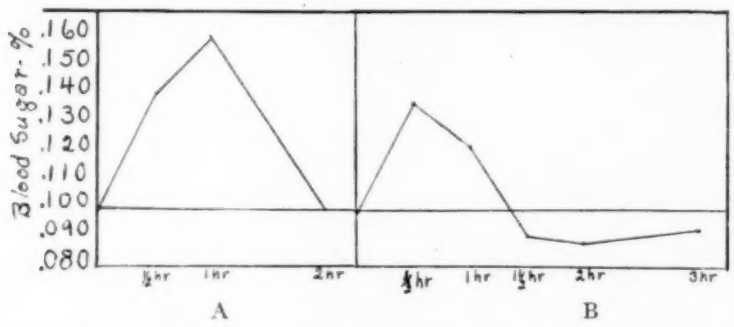


Chart 4.—Normal blood sugar tolerance curves. *A* indicates the normal curve taken from Todd's "Clinical Diagnosis," 1923, p. 368; *B*, normal curve, suggested average from recent work.

CONCLUSION

It would seem, then, that in schizophrenia and in the amyostasis of late epidemic encephalitis, as well as in certain noninfectious types of striate disorder, a certain resemblance exists from the standpoint of blood sugar tolerance reaction. This from the physiologic point of view affords further evidence of a certain likeness in part of basic pathology, the same in the case of schizophrenia probably being phasic[24] in character. This pathologic similarity, on the basis of clinical resemblance and histopathologic research, it is probable may be neuraxial in site, although possibly secondarily at least marked by a common asso-

22. Folin and Berglund: J. Biol. Chem. **51**:213, 1922.

23. Schwab, S. I.: Diagnostic Value of Blood Sugar Curves in Neurology, Arch. Neurol. & Psychiat. **8**:401 (Oct.) 1922.

24. Raphael, T.: Am. J. Psychiat. **2**:515 (April) 1923.

ciated hepatic dysfunction from the standpoint of influence on carbohydrate metabolism, as suggested by Halliday [20] and Marghreth [25] for encephalitis and by one of us [11] for schizophrenia.

Through this work, too, support is afforded the concept of higher centers controlling metabolic processes [26] supplying a possible basis of explanation for much of the generally noted metabolic and vegetative abnormality observed in schizophrenia and in certain other mental disorders, more especially the manic-depressive psychoses. It is conceivable that from this point of view the specific differences in sugar tolerance reaction noted between the depressed phase of the latter disorder and schizophrenia, the general response in both being basically alike, may be dependent on specific differences in basic or constitutional physiologic pattern. An interesting field of speculation is also opened up as to the actual nature of this possible central disturbance in schizophrenia, its relation, primary or secondary, through cortical effect, to the general picture of the disorder as presented psychiatrically, and its bearing from the standpoint of constitution as a predisposing factor.

---

25. Marghreth, G.: La glicemia nelle sindromi parkinsoniane postencefalitiche e nel morbo di Parkinson, Rif. med. **41**:1 (Jan.) 1925.

26. Glaser, F.: Serum Calcium in Neuroses and Fever, München. med. Wchnschr. **72**:331 (Feb.) 1925; abstr. J. A. M. A. **84**:1391 (May) 1925. Cannon, W. B.: Evidence of Nervous Control of Some Internal Secretions, Arch. Neurol. & Psychiat. **6**:707 (Dec.) 1921. Dercum, F. X.: The Thalamus in the Physiology and Pathology of the Mind, ibid. **14**:289 (Sept.) 1925.

Clinical and Occasional Notes

THROMBOSIS OF THE ROLANDIC VEIN: REPORT OF CASE

CHARLES EDWARD DOWMAN, M.D., ATLANTA, GEORGIA

So far as I can learn, there is no recorded case of thrombosis of the rolandic vein. The apparent rarity of the condition and the interesting localizing symptoms and findings justify this report. It is interesting to note that in the case to be reported a preoperative diagnosis was made of tumor of the right parietal lobe or a thrombosis of the right rolandic vein. The latter possibility was kept in mind because of similar findings which developed after the ligation of the rolandic vein in a patient whose third ventricle was explored.[1]

History.—D. C. H., a white man, aged 37, referred by Dr. J. E. Paullin, was admitted to the Piedmont Hospital on March 18, 1925. The family history was unimportant. His health had been good up to March 6, 1925, when he became conscious of a twitching sensation in the right upper eyelid. This sensation lasted five seconds and was followed by an attack of dizziness lasting six or seven seconds which was so severe as to cause him to hold on to something to keep from falling. During the following three or four days he had from twelve to fifteen such attacks daily. There was never any actual muscular twitching of the eyelid, but only a sensory phenomenon. On March 11, 1925, a sensation of numbness appeared in the left hand, which gradually extended over the whole left arm and into the left side of the neck and lower portion of the left side of the face. This numbness persisted, and on March 18 had involved the left side of the body and to a certain extent the left leg. The patient noticed that in spite of the numbness the sensation to touch was not absent but only decreased in intensity. As the arm began to feel numb, awkwardness of movements of the affected extremity developed. Since March 10, 1925, there had been several attacks of headache, the pain being more severe in the right parietal region. The attacks of dizziness ceased after the development of the numbness.

Neurologic Examination.—This gave the following positive findings: (1) slightly unequal pupils, the right being larger than the left; (2) the history of numbness in the lower part of the face on the left side, but no sensory disturbance on test; (3) a distinct weakness of the left hand grip and diminished strength in the flexors and extensors of the left forearm; (4) subjective numbness in the left hand and arm, but no marked disturbance of sensation to touch or pin prick, although these sensations were slightly obtunded as compared to those of the right side; (5) a complete loss of ability to recognize objects placed in the left hand (astereognosis); (6) a loss of joint sense in the fingers of the left hand; (7) a loss of the sense of position of the left arm and left leg; (8) a lack of recognition of the two points of a compass beyond the normal when two points are simultaneously touched on the left arm and hand; (9) an inability to distinguish between cloths of fine and coarse texture when placed in the left

1. Dowman: Report of a Case of Inflammatory Occlusion of the Foramina of Monro, With Marked Increase of Intracranial Pressure, Relieved by Operation, Piedmont Hosp. Bull. **1**:11 (Oct.) 1924.

hand; (10) an inability to distinguish slight differences in the weight of objects placed in the left hand; (11) sluggish left abdominal reflexes; (12) exaggerated left deep arm and leg reflexes.

Physical Examination.—The findings were normal with the exception of moderate pyorrhea and a slight impairment of percussion note over the left apex. The routine blood and urine examinations and the chemical examinations of the blood gave findings within the normal limits. The roentgen-ray examination of the skull and vertebrae showed nothing abnormal.

The impression after a thorough examination, as written on the patient's record, was as follows: "This patient has a definite lesion of the right parietal lobe, with some slight involvement of the right precentral area. The rapidity of the onset of the symptoms is rather unusual for tumor. In spite of this, however, it is felt that the diagnosis of tumor of the right parietal lobe is entirely justifiable. If a tumor is present the rather acute symptoms may have been caused by a recent hemorrhage, or cystic changes in the tumor. A thrombosis of the right rolandic vein may cause a similar neurologic picture. One would naturally think that if this latter condition were present, the symptoms, instead of becoming more pronounced, would by this time begin to recede. It is felt that an exploratory craniotomy should be made."

Operation (March 20, 1925).—Under 1 per cent. procain-epinephrin infiltration anesthesia, a bone flap was laid down so as to expose the right rolandic region. A dural flap was reflected upward, thereby exposing the underlying brain. There was no evidence of a tumor being present. The convolutions of the brain were somewhat smaller and harder than normal. There was an excessive amount of subarachnoid fluid in the sulci. The rolandic vein was very large and bluish black. It was hard to the touch and could be rolled under the fingers. The vein had the appearance of containing an extensive clot. The neighboring cortical veins were greatly distended but were not firm to the touch as was the rolandic vein. The diagnosis of thrombosis of the rolandic vein seemed definitely verified without actually cutting into the vein. There was evidently a compensatory dilatation of the neighboring veins. The dura was closed with fine silk sutures, the bone flap replaced and the scalp wound sutured.

Course and Result.—The patient's convalescence from the operation was uneventful. About eight or ten days after the operation he began to note marked improvement in the left arm and hand. This improvement continued from day to day. On April 6, 1925, the following note was made: "The left hand grip is still weaker than the right but is much stronger than before the operation. The loss of the sense of position of the left arm is enormously improved, although there is a slight amount of waving of the left hand when both arms are rapidly pronated and supinated. The patient is able to recognize objects placed in the left hand and knows the position of the fingers when passively flexed and extended."

When the patient was seen on April 24, 1925, there were no neurologic manifestations. At times there was a slight amount of subjective numbness in the left hand. Since leaving the hospital there has been a gain of 7½ pounds (3.4 kg.), and the patient claims to feel as well as he ever felt.

COMMENT

Parietal lobe lesions are comparatively easy to diagnose if one remembers that in the cortex of this region are located the so-called "psychotactile" sensations, and a lesion of this area gives rise to a disturbance of these sensations in the contralateral extremities. All gross sensations, such as touch, pain, the

recognition of heat and cold and the primitive emotions are registered in the optic thalamus, whereas the higher discriminating sensations are relayed up to the cortical centers behind the rolandic fissure. By discriminating sensations are meant: the ability to appreciate such spatial relations as length, breadth and thickness, the differences in the weight of objects felt, the position of the joints of the fingers and toes, the appreciation of the difference in the texture of cloth, the recognition of objects felt, the knowledge of the position of the extremities, etc. These more refined sensations are therefore rightfully called "psychotactile." A parietal lobe lesion will cause a disturbance or loss of these sensations without interfering materially with the primitive sensations of touch, pain, etc.

In the case under discussion the findings noted pointed conclusively to the right parietal lobe as the site of the lesion. A thrombosis of the main vein draining these centers would naturally interfere materially with the proper function of the cortical cells. As the venous circulation became reestablished either through the neighboring veins or through a canalization in the existing thrombus, the affected centers should again resume their function and the symptoms and findings should disappear. Such a result it seems has already occurred in the case reported. The operation was of value only in excluding a possible tumor, although it may be argued that the exposure and manipulation of the involved brain hastened the reparative process. Why a thrombus should have occurred in this particular vein is a question which I am unable to answer.

News and Comments

CONGRESS OF ALIENISTS AND NEUROLOGISTS OF FRANCE AND OF FRENCH SPEAKING COUNTRIES

The thirtieth session of the Congress of Alienists and Neurologists of France and of French Speaking Countries will be held at Geneva and Lausanne from Aug. 2 to 7, 1926. It will coincide with the celebration of the centenary of the death of Pinel.

Presidents: Professor Long, of Geneva; Dr. René Semelaigne, of Paris.

Vice President: Professor Raviart, of Lille.

General Secretary: Dr. Repond, Medical Director of the Maison de Santé de Malevoz-Monthey (Valais).

The following subjects have been selected by the general assembly of the congress for special discussion.

Psychiatry: "Schizophrenia." Speakers: Professor Bleuler, of Zurich, and Professor Henri Claude, of Paris.

Neurology: "Babinski's Sign: Characteristics, Mechanism and Significance." Speaker: Dr. Tournay, of Paris.

Assistance: "The Treatment of Mental Diseases by Work." Speakers: Professor Ch. Ladame, of Geneva, and Dr. Demay, Chief Physician of the Asylum at Clermont (Oise).

Abstracts from Current Literature

THE PATHOLOGIC ANATOMY OF ENCEPHALITIC PARKINSONISM. LESLIE B. HOHMAN, Arb. a. d. Neurol. Inst. Wien. Univers. **27:1** (May) 1925.

This contribution is based on a careful clinico-anatomic study of eleven cases of parkinsonism associated with or following encephalitis. Histologic examination showed intense parenchymatous changes in the brain in all the cases. The ganglion cells showed various forms of degeneration. Surprisingly, acute swellings were entirely or almost entirely absent; in the cases in which they were present, they were so slight that no significance could be attached to them so far as the clinical picture was concerned. The acute changes seemed to have been due to the effects of a severe disease which had terminated fatally. Another change which could also be looked on as a complication of a severe and debilitating disease was a lipodystrophy that could be seen in practically all the microscopic sections. This the author attributes to nutritional disturbances. The lipodystrophic changes were not general, i. e., they did not affect all cells of the nervous system but only the large motor cells of the bulbar nuclei, the dentate nucleus, the cells of the olive and those of the striatum. Hohman suggests the possibility that the lipodystrophic degeneration is an expression of presenility.

In addition to the trophic disturbances, the cells also showed other evidences of degeneration, such as rarefaction with a breaking down of nuclei and a total disappearance of some of the cells. Some of the cells were unusually pale and vacuolated. None of the cellular changes could be looked on as a characteristic pathologic feature of the disease. It was noteworthy, however, that one could find in one and the same case chronic cell changes, lipodystrophic and sclerotic in nature, associated with evidences of severe acute cell degeneration.

It was extremely difficult to explain the mechanism of the pathologic changes observed. One section from a given brain would show such severe cell changes without any evidences of inflammation that the entire pathologic process would have to be regarded as one of a toxic parenchymatous degeneration; the next section from the same brain would show similar degenerative changes associated with evidences of an acute inflammatory process (lymphocytes, plasma cells and rod cells, with here and there a leukocyte). In view of these findings, one might conclude that the process was inflammatory with a predominance of degenerative changes of the same nature as are encountered in chronic inflammatory conditions.

The substantia nigra in all cases was apparently free from severe degenerative cell changes; the cells did not appear acutely swollen, but were unusually pale, with their margins broken up, so that the cell pigment having migrated from the cell body could be seen to form clumps and clusters which entered into the tissues and capillaries. The glia cells in this area also contained many clusters of pigment.

The nerve fibers showed the following changes: Some appeared to be merely swollen; this could best be seen in areas in which the pathologic process was not very far advanced, such as the cerebral cortex. Other areas showed broken-down fibers; this breaking down, however, was not en masse, but was a gradual process which also seemed to have involved the axis

cylinders. Although the process was partially a diffuse one, it bore no resemblance to that usually noted in multiple sclerosis; it was more in the nature of a process of discontinuation, such as is encountered in senile conditions, except that it bore no topographic relationship to the vessels. It was an indistinct patchy dysmyelinization, which occasionally leads to the formation of the so-called status marmoratus. Another type of nerve fiber change was observed near the blood vessels; here one could find changes varying from the slightest to the severest degree of parenchymatous disintegration — a perivascular disintegration of nerve fibers. A similar type of fiber disintegration could also be seen in the supporting structure; in some areas this was followed by a "falling out" of complete masses of fibers, leading to the formation of the so-called status cribratus. Although these fiber degenerations affected mostly the delicate fibers in the cortex and those in the ganglia, they were not absolutely limited to these structures but could also be observed in the coarser fibers in the region of the striatum and internal capsule — the fibers thus involved were those usually included in the frontothalamic system. The reaction of the surrounding tissues to these various types of fiber degeneration was rather slight, there being only a scanty accumulation of fat granules. The entire process, so far as the fiber changes are concerned, could be looked on as a chronic progressive degeneration, which, owing to its gradual mode of onset, gave rise to only slight reactive phenomena.

The glial reaction to the parenchymatous lesions in the cells and fibers was relatively mild; this the author attributes to the fact that the glia itself was affected by the pathologic process. One must not, however, gain the impression that glial changes were entirely absent. Glial changes were registered in the slight and limited formation of fibrillae, with here and there some perivascular sclerosis, as in senile sclerosis. The glia also showed an increase in satellite cells arranged in longitudinal rows along the vessels, partly surrounding the cells and partly adhering to them — a typical neuronophagia. Plasma cells were rarely seen.

As in other diseases with such extensive pathologic changes, the mesenchyma also participated in the process. Here were seen presenile vascular changes, hyaline degeneration and dilatation of the blood vessels. Typical vascular sclerosis was found in the brains of patients who had not reached their fiftieth year. These changes, however, are not regarded as primary. The meninges showed evidences of slight irritation in the form of moderate proliferation due to the inflammatory process.

It was difficult to decide whether the infiltrates in the nerve tissue were purely gliogenous in nature, or whether they consisted of lymphocytes and round cells. The infiltrates were not always perivascular, some of them were diffusely scattered and bore no relation to the vessels; in the latter case, it was almost impossible to establish their character. Rod cell, small glial elements, lymphocytes and plasma cells could almost always be found; leukocytes were extremely rare. The entire picture gave one the impression of a chronic type of inflammation. The usual hemorrhages reported by so many previous observers, were strikingly absent in all of the author's cases. The latter, therefore, believes that these hemorrhages are probably terminal manifestations, resembling those frequently observed in pneumonia, and other infectious diseases and that they are not pathognomonic of encephalitis.

Hohman summarizes his conception of the entire process as a chronic progressive degenerative inflammation which is frequently associated with changes in the nature of a premature marasmus.

As to the localization of the pathologic process: There is no doubt that the process is a diffuse one involving the entire central nervous system, although occasionally areas are found in which the manifestations are so slight that they might easily be overlooked. It is also of interest to note that in the chronic cases the large motor cells often remain intact — they seem to possess a relative immunity to the process; this, however, is not invariably so, because in some areas, notably in the mesencephalon (basal ganglia, optic thalamus) some of the large cells seemed to have been severely affected by the acute component of the pathologic process. It must also be emphasized that every one of the author's cases showed, in addition to the involvement described above, changes in the cerebral cortex and in the deeper parts of the cerebellum, especially in the dentate nucleus.

From the point of view of intensity of the pathologic process the structures may be said to be involved in the following order: substantia nigra, striatum, pallidum and midbrain ganglia, dentate nucleus, cerebral cortex, medulla oblongata and spinal cord. Individual nuclei may be severely affected, especially the olive and the locus caeruleus. The greater involvement of one area than another cannot possibly be due solely to a difference in the iron content of the respective tissues; the iron content of the substantia nigra is about the same as that of the pallidum, but the former is, as a rule, much more severely affected than the latter. Nor can this difference in intensity of involvement be attributed to any peculiarity in the vascular supply of these parts; areas of tissue supplied by different blood vessels were found to be affected simultaneously and with the same intensity. Only one factor is of great significance in this connection, and that is that the disease is almost invariably symmetrically bilateral, even though there may be some differences in the extent of the symmetry.

The next problem discussed is whether the pathologic process is the result of the primary disease. Clinically, the cases showed that in some of them the parkinsonism began directly with the onset of the primary disease and kept on progressing gradually but uninterruptedly; in other cases there was a relatively free interval between the onset of the disease and the development of the parkinsonism. On purely anatomicopathologic grounds the reason for the difference in the mode of onset of the parkinsonism in these two groups of cases could not be explained satisfactorily. Hohman is, therefore, inclined to attribute this latency in the appearance of the parkinsonism to a regression of the inflammatory process. The entire pathologic process does not speak for a steplike progression of the disease, as in multiple sclerosis; it seems to be more in favor of a gradually progressing chronic inflammation, because the steplike progression is not evident in the clinical picture in most of the cases, even though here and there one does encounter a case with an apoplectiform type of progression. The author also believes that the latency in some of the cases is merely an apparent interruption of the disease, and that it is not an expression of renewed attacks of inflammation; the process is a chronic progressive one from the day of infection, and the intermissions are merely clinical phenomena with no adequate pathologic substratum at their basis.

In view of the diffuseness of the pathologic process it is also difficult to correlate the clinical symptoms of encephalitic parkinsonism with any definite localization of the lesions. Clinically, the author's cases presented three groups of manifestations: hypertonia, akinesia and tremor. Tremor was the one symptom that was not present in all cases, whereas hypertonia and akinesia were found in every one of them. To illustrate the difficulties of the problem,

he cites two cases, in one of which, with marked hypertonia, the pallidum showed only the slightest degree of involvement, whereas the substantia nigra was severely affected; at first sight, this would seem to indicate that pallidal lesions alone do not give rise to hypertonia. On the other hand, in this case the striatum was more affected than the pallidum. A similar relationship, although not perhaps as clear cut, was also observed in other cases, i. e., lesser involvement of the pallidum and greater involvement of the substantia nigra. Another observation noted was this: In some cases the hypertonicity was relatively less marked than in others; anatomically the substantia nigra was better preserved in the former than in the latter. This would lead one to conclude that the substantia nigra is perhaps of greater significance than the pallidum so far as hypertonia is concerned. Similarly, Wilder reports a case with a sudden onset of the parkinsonism, in which lesions were found only in the substantia nigra. Hohman, therefore, does not wish to imply that he would entirely exclude the pallidum as a genetic factor in the production of hypertonia, but he believes that the lesions in the substantia nigra are the principal factor.

As to the akinesia: The prevailing notion today seems to be that any muscle may show loss of spontaneity and poverty of movement, but that the mechanism for these phenomena must be sought in a disturbance of the cortical pathways. Here too, however, one cannot be certain as to the correctness of this conception, because one series of the author's cases showed definite involvement of the frontothalamic systems, whereas in another series these systems were found to be intact. According to Riese, the coarse centripetal and delicate centrifugal fibers in the striatum and pallidum connect these structures with the subcortex. The sections examined by Hohman showed that most of the coarse fibers were intact or almost so, but that in no case were the delicate fibers free from involvement. It must, therefore, be assumed that the frontothalamostriatal fibers have nothing to do with akinesia, but that the akinesia might be due to a disturbance in the centripetal impulses, as a result of which these never reach the cortex. As all the cases examined showed changes in the cortex, especially in its delicate fibers, one might perhaps be justified in attributing the phenomena of akinesia to the lesions found in the cortex.

As to the tremor: Any attempt to differentiate the cases with tremor from those without tremor must take into consideration the cerebellar mechanism. Surprising as it may seem, the cases with tremor in Hohman's series, showed little cerebellar involvement; this involvement was limited to the dentate nucleus; but as this nucleus was affected in all cases, one cannot assume that in the cases in which the lesion was not very severe it was the cause of the tremor. This also applies to the pallidum, because in some of these cases the pallidum was only slightly involved, whereas the large as well as the small cells in the striatum and in the mesencephalon were severely affected. Here too, then, it is impossible to distinguish the cases with tremor from those without tremor on the basis of the intensity and location of the pathologic process.

All these findings, according to Hohman, would seem to show that the pallidum syndrome so ingeniously elaborated clinically by Förster and Hunt cannot be substantiated anatomically, at least not in cases of parkinsonism, because although the clinical features of encephalitic parkinsonism may be said to be indistinguishable from those of paralysis agitans, the pathologic process in the former is entirely different from that in the latter. The tendency, therefore, to attribute both diseases to a localization in the pallidum is not

well founded, because in encephalitic parkinsonism an entire series of different factors are at work than is the case in paralysis agitans.

The foregoing investigations would seem to show the futility of attempting to determine the pathologic process of a disease of this kind unless the entire central nervous system is subjected to a most painstaking and thorough histologic examination. They also show the difficulties of localization in a pathologic process as diffuse as that of encephalitis. As a matter of fact, similar difficulties are encountered even in local lesions (such as hemorrhage, softening) when they occur in senile persons, because the senium itself, may in addition to the local process give rise to such diffuse lesions that it becomes almost impossible to correlate the clinical symptoms with the lesions found at necropsy. This must especially be borne in mind in attempting to localize a cerebral neoplasm, when, no matter how small it may be, it has already produced general symptoms of brain tumor.

KESCHNER, New York.

THE CLASSIFICATION OF CEREBRAL TUMORS. ROUSSY, LHERMITTE and CORNIL, Ann. d'anat. path. med.-chir. **1**:333, 1924.

The present classifications of cerebral neoplasms are founded on embryologic concepts, although these must not be taken too seriously since they rule out the pathogenesis, embryologic displacements and traumatic factors, and commit one to the "dysembryoblastic" theory of tumor formation. A short discussion of the histogenesis of the central nervous system is followed by a similar one on the cytology, histology and regional variations of the neuroglia. The authors divide tumors of the interstitial tissue of the brain into (1) astrocyte gliomas or astrocytomas; (2) cellular or nonfibrillar gliomas, including such varieties as the round cell, spindle cell, polymorphic, and ameboid cell gliomas; (3) glioblastomas and spongioblastomas or ependymogliomas.

The astrocytoma, the most common tumor, is composed of cells which retain many characteristics of adult neuroglia. The cytoplasms of the constituent cells contain from two to thirty glia granules; the nucleus, generally rounded, sometimes elongated, seldom mitotic, has a very distinct chromatin network. In various locations, very large degenerated cells are often seen. Neuroglia fibers are seen in great abundance, especially in the hard or fibrous tumors. Nerve cells and fibers may be found within the confines of the tumor. The mesodermic tissue is increased, with the presence of large almost cavernous blood vessels. Thromboses, hemorrhages and other degenerations are by no means rare. There is no reciprocal mutation between ectodermic and mesodermic tissue, however. The collagen, at times found in large amounts, is laid down both by the physiologic activity of the perivascular sheaths and by precipitation of certain proteins in situ. The vessel walls often undergo hyaline or even calcareous degeneration.

The nonfibrillar gliomas comprise two main types, those with round cells and those with spindle cells as a basis. The small round cells are distinguished from lymphocytes by their paler nuclei. The whole tumor is composed of these cells and much resembles the small round cell sarcoma, which arises in the brain only as a metastasis. Blood vessel walls are very thin, though not seldom hyalinized. The spindle cell glioma is even more apt to be confounded with sarcoma, although the separation has been accomplished satisfactorily by the use of elective methods of impregnation. The cells of this tumor are united in a vast syncytium within which the cell boundaries are no longer recognizable. The slender nuclei, pale, with few chromatic

granules, never take on extraordinary proportions. Arranged parallel with one another, the cells are gathered in large sweeping bundles which run in different directions. In other locations the groundwork may appear reticular, with stellate cells, anastomosing with one another. This tumor is found most frequently on the cranial nerves.

The polymorphic cell glioma is recognized by the wide variation in the types of cells present and by the occurrence of giant forms. In these last the nuclei can sometimes be seen joined to one another by fine chromatic bands, recalling the structure of the polymorphonuclear leukocyte.

The ameboid cell gliomas are distinguished from the preceding by their cellular structure. These elements have an abundant cytoplasm, with long branching projections often joined to expansions of neighboring cells. The cytoplasm is clear, often vacuolated, containing fat globules, products of disintegration of the myelin sheaths, and other granules. Nuclei are situated eccentrically, small, dark, with a definite nuclear membrane. These tumor cells extend into the surrounding tissue without definite limits, the neoplastic cells coming to resemble more and more the normal tissue cells until they merge directly with the normal neuroglia.

Degenerative processes are often observed in all gliomas. These comprise hemorrhages from the large cavernous delicate vessels, colloid degeneration and cyst formation. The latter is due to the colloid degeneration of both cell and stroma in the tumor.

Tumors of the ependyma and choroid plexus can be differentiated when the cells have reached adult type, but since they spring from the same cell, that lining the neural canal, the differentiation of less developed forms is often difficult. These tumors arise in the juxta-ependymal region, and often when no tumor exists we may find enclosed in the nervous substance some acini and rosets, probably snared off from the ependyma in the vicinity.

An interesting section is devoted to the cerebral lesions arising as a consequence of the development of gliomas in the brain. The glioma itself destroys the nerve tissue only slightly, not nearly to the extent that a vascular lesion does. Rather it displaces the nervous tissue. Even the compression, however, is harmful in the end, probably by bringing about interference with the blood supply. In the second place the tumor can work with destructive effect by altering the circulation of the cerebrospinal fluid, especially that flowing about the individual cells. Even so, the degenerations are much less marked than one would expect from the volume of the tumor. The production of hydrocephalus and displacement of the basilar structures through the foramen magnum are touched on, but more particularly the lesions in the vicinity of the tumor. On fresh section the pallor and flattening of the convolutions is to be remarked, then the brownish discoloration, the disappearance of the subarachnoid space. Under the microscope the nerve fibers are found swollen, with fragmentation of the myelin and thinning of the sheath. Fat may be abundant, as a result of myelin destruction. At other times the sheath is swollen, the interstitial tissue manifests a very notable reticulum, and ameboid cells proliferate and take up the products of disintegration. Perivascular spaces are dilated and contain phagocytic cells, especially polyblasts, but no plasma cells. The ganglion cells in the vicinity show chromatolysis, displacement of the nucleus, condensation of the dendrons, and often very marked satellitosis. Such cellular changes are often found at a considerable distance from the neoplasm and may explain the psychic symptoms, especially the progressive deterioration. Whether they are due to intoxication from the by-products

of metabolism of the tumor cells, or to interference in nutrition cannot be answered positively.

Certain tumors in the central nervous system undoubtedly spring from the nerve cells. Although adult nerve cells never proliferate, yet the immature ones possess this capacity, and from them spring certain rare tumors, the ganglioneuromas, the neurogliocytomas, the neuroblastomas and so on. In these tumors are found rather large cells with more or less the appearance of chromophilic granules, intracellular fibrils and budding axons, all in a primitive stage of development. Grossly these tumors resemble the ordinary gliomas. Closely allied to these remarkable tumors are the congenital malformations, such as disseminated cortical histio-atypia, tuberous sclerosis, pseudosclerosis, etc.

Tumors developing from the cranial nerves have been considered as fibromas, or neuromas. The most common are those developing on the acoustic nerve. These spring from the peripheral neuroglia which, outside the cranial cavity, become the cells of Schwann. Since it has been shown that the so-called neuromas in the peripheral nerves arise from the cells of Schwann, they may well be termed peripheral gliomas. The same holds true for the tumors developing on nerves within the cranial or spinal cavity. The tumors resemble the fusiform gliomas in practically every detail.

When multiple tumors spring from the nerves, the question of simultaneous origin or metastasis arises. When the tumors are of approximately equal size, as often happens in the acoustic area, they may be considered as independent; when, however, there is a multitude of such small tumors, metastasis by way of the spinal fluid is more likely. This condition is closely allied to the "neurofibromatosis" of von Recklinghausen, although the prognosis is much less favorable.

A considerable and useful bibliography is appended.

FREEMAN, Washington, D. C.

THE TWO DIVISIONS OF THE INTERNAL GRANULAR LAYER (BRODMANN). R. BÁRÁNY, J. f. Psychol. u. Neurol. **31**:289 (June) 1925.

In man the optic nerve fibers from the lateral half of the retina enter the optic tract uncrossed, while the fibers from the mesial half decussate at the optic chiasm. The literature abounds in numerous discussions as to the position of the crossed and uncrossed fibers in the the optic nerve and tract. In 1920, Minkowski was able to demonstrate precisely the termination of these fibers in the external geniculate body—the primary end-station of the optic nerve fibers. After monocular enucleation in various animals, he studied carefully the resulting secondary degenerations in the external geniculate bodies. He found that both in man and monkey the external geniculate body consisted of a series of cellular layers separated from each other by myelinated lamellae which were formed by the "afferent" optic nerve and "efferent" optic tract fibers. He established definitely that within the external geniculate body the crossed optic nerve fibers are sharply separated from the uncrossed fibers. Physiologically, as well as psychologically, it is certain that binocular impressions do not occur in the geniculate body. The impressions of homonymous retinal elements may be either completely similar, in which case a binocular impression resembles a monocular one, or they may be dissimilar, so that there results either an exclusion or an admixture of both impressions. The exclusion, the similarity of the binocular and monocular impressions could still be

explained by the structure of the geniculate body. Binocular admixture, however, cannot possibly take place in the geniculate body, because here there is no room for an admixture, all cells subserving both monocular impressions. At the same time it must also be borne in mind that there is no apparatus for association in this body between the layers of the crossed and those of the uncrossed fibers. From this one must conclude that the admixture of the crossed and uncrossed impressions does not occur until the latter have reached the cortex. If this be so, the next question that presents itself is, which part of the cortex contains the anatomic substratum for this admixture? In both man and monkey there exists a well marked line of demarcation which divides the internal granular layer of the cortex in the calcarine fissure into two equal parts. This line of demarcation is the so-called stria Gennari, which contains not only fibers of the optic radiation (Cajal), but also short association fibers. This was confirmed by Monakow, who could find no actual atrophy of this stria in persons who have been blind since earliest childhood. Cajal also established the fact that the fibers of the optic radiation terminate in the internal granular layer. The simplest and most practical way in which the images conveyed by the crossed and uncrossed fibers could fuse would be for the elements stimulated by both sets of fibers to be superimposed over each other; no fusion could ever occur if these elements were in juxtaposition instead of superimposition; the resulting image, according to Wilbrand, would then assume a chess board pattern. The author believes that such a simple arrangement (superimposition of the elements) actually exists in the visual cortex of man and monkey. The next step would be to assume that both parts of the lamina granularis interna are the anatomic representation of both monocular images. If this assumption is correct, one would expect that in animals without uncrossed optic nerve fibers the lamina granularis would consist of only one layer. In the lower mammals (guinea-pigs) the uncrossed portion of the optic nerves is unusually small, most of the fibers being crossed, and Brodmann has actually shown that in these animals there exists only one granular layer (the lower), with the stria Gennari over it. The guinea-pig has very little binocular vision. The lateral implantation of its eyes is marked. Animals with complete lateral implantation of their eyes and complete optic nerve decussation would seem to be ideal subjects for the investigation of this condition. It would, therefore, be of great interest to determine whether, after all, the guinea-pig does not show somewhere a small area with a double layer of the internal granular layer. As a matter of fact, Minkowski found that the external geniculate body of the cat contained a considerable area for uncrossed fibers. But neither Cajal nor Brodmann could find a double granular layer in this animal. Perhaps further investigation will show the existence of a double granular layer in some area which could explain its relation to the corresponding parts of the retina as well as to binocular vision.

Another significant fact, which could be confirmed anatomically, would be the finding in man and monkey of an unusually well marked double internal granular layer in that area of the calcarine fissure which corresponds to the macula. If this is true, then one would also expect that the human visual cortex corresponding to the temporal "sickle," the part in which binocular vision does not occur, is devoid of a double granular layer. Naturally only a positive result would prove the correctness of such an hypothesis, because other factors determining anatomic structure may and also probably do exist.

From what has thus far been said, one might conclude that the superior part of the granular layer, i. e., the part immediately subjacent to the surface

of the cortex, is the terminal station of the uncrossed fibers, because in animals without doubling of the granular layer and with predominatingly crossed optic nerves, the internal granular layer lies immediately beneath the stria Gennari. Furthermore, one could also assume that within the monocular visual field the six fundamental colors (red, green, blue, yellow, white and black) are not in juxtaposition but are superimposed over each other, so that fusion of these various colors may also occur. Wilbrand and Saenger believe that such superimposition of colors is actually represented in the various layers of the visual cortex, because in cortical hemorrhages vision for colors may be lost while ordinary vision (for light) is preserved. These observers are of the opinion that the centers for colors are superimposed over those for the perception of light, and that the former are more affected by pressure from cortical hemorrhage, and are therefore paralyzed much earlier. Assuming that the various colors are superimposed over each other, the reason for the existence of a considerable number of cellular layers within the internal granular layer becomes evident.

The likelihood of the truth of the foregoing hypotheses as to the significance of the upper and lower parts of the granular layer as the end stations for the crossed and uncrossed fibers can be subjected to further proof. As there is no subjective difference between homonymous visual fields, it would be necessary for both parts of the granular layer to be identical in structure, i. e., that both parts would have to contain the same number of cells and the same associations. In order to study this structure in detail, both parts of the granular layer would have to be examined by the Golgi method—and this has not as yet been done—although the Nissl preparation shows that there is an actual difference between these layers, the lower being much richer in cells than the upper. This would seem to show that the foregoing hypothesis is not true, and it must therefore be assumed that fusion of the two monocular images occurs in a "mixed field," and that the upper part of the granular layer is to be regarded as the "mixed field" whereas the lower part is to be regarded as the area which contains both monocular visual fields superimposed over each other. In view of this, one would also be justified in regarding the division of the granular layer into two parts as an expression of binocular vision, because a "mixed field" is necessary only in binocular vision. Of great interest in this connection would also be a study of secondary degeneration in animals following unilateral ocular extirpation.

In conclusion Bárány states that he is fully aware that he is presenting a mere hypothesis, but that he has submitted his ideas to Minkowski who believes that they are probably correct, and that Professor Henschen is also of the same opinion. He is publishing another paper with a great mass of details on the same problem, and he hopes that both of these contributions will stimulate other investigators to similar research in this direction. He also states that to the best of his knowledge this hypothesis is the first attempt "to animate functionally the anatomic structure of the cerebral cortex."

KESCHNER, New York.

STUDIES ON APHASIAS. ANATOMIC AND CLINICAL CONTRIBUTION TO THE DOCTRINE OF CEREBRAL LOCALIZATIONS. AGOSTA ALDO, Rassegna di Studi Psichiat. **8**:3-144. (Jan.-April) 1924.

In this anatomic and clinical study, which has been awarded a gold medal, the author describes twenty-eight cases of aphasia with necropsy. These are divided into five groups: sensory or perceptive aphasias; total aphasias; trans-

cortical or associative aphasias; conduction aphasias, and motor aphasias. Each of the five groups is thoroughly discussed in the light of previous investigations and of the author's own findings. Henschen's classic work on aphasia is amply quoted. A brief summary follows the presentation of each group of cases and, after a comprehensive chapter on the centers and pathways of speech, a general summary closes the article.

Regarding the sensory aphasias, the author points out that the so-called conduction pathways of speech run neither in the inferior longitudinal tract, through the uncinate, nor through the insula; they pass above the last. He shows that left temporo-parieto-occipital lesions, even when extensive, disturb but do not suppress the function of speech, not even echolalic speech. Compensatory reestablishment of function must take place by way of pathways which connect the right acoustic centers with the left motor center through the splenium, since compensation through the right hemisphere alone is not possible. Such compensatory functions can be established rapidly; therefore, the conception of a Wernicke center for the understanding of speech, an autonomic, unilateral center in which images are stored up, is not correct.

From the study of the second group, the author concludes that total aphasia may result either from a single lesion destroying the zone of white substance situated above the lateral ventricle and the lenticular nucleus of the left side, or from any of the following double lesions: (*a*) bilateral lesions in the posterior association areas preventing the stimuli from reaching the motor zones of speech; (*b*) lesions of the left temporoparietal region and of the splenium; (*c*) lesions of the left temporoparietal and left operculorolandic region.

The cases of the third group demonstrate the existence of transcortical aphasias. Such syndromes are due to a lesion in the left centrum ovale and appear only when the deeper associative bundles are involved. The prefrontal centrum ovale in its lower and outermost portion is related to the speech function, especially to the symbolic comprehension and the spontaneous evocation of speech. The author, however, does not maintain that the field of comprehension is there located; he merely states that integrity of the great left fronto-occipital bundle, in its whole course, is essential for the conscious evocation of words and the perception of their symbolic significance.

The existence of conduction aphasias is shown both clinically and anatomically by the cases of the fourth group. The author thinks that the conduction aphasias, manifested almost purely by paraphasia and paragraphia should be called praxic aphasias. The anatomic basis of this form of aphasia is represented by lesions in the borderline region between the insula and the centrum ovale. Therefore, the praxic pathways of speech and writing must be identified with the arcuate bundle.

In the analysis of the fifth group (motor aphasia), the author agrees with other investigators that lesions of the lenticular zone do not produce aphemic disorders, even when the anterior portion of the left putamen is involved. He also agrees that lesions limited to the lower third of the ascending frontal convolution produce in right handed individuals transient speech disorders; that lesions in any part of the arcuate tract produce aphemia, complete or incomplete according to the degree of the lesion, and that lesions of the left callosal radiations render the aphemia permanent. He concludes also that the motor function of speech is fatally disturbed with lesions of the white substance underlying the Broca center (extended to include the operculum rolandi,

the foot of the third and second frontal convolutions) at the point in which the fibers of the arcuate bundle cross the callosal radiations. Judging from the facility of compensation for cortical lesions and from the permanence of aphasia after deep lesions, he inclines to the opinion that speech is eminently an associative function.

The general conclusions of the author are: Today, a middle course is possible between the unjustified skepticism of the opponents and the fantastic constructions of extremists for localization. The Wernicke conception of a cortical center for the understanding of speech, in which the images of words are stored up and from which they may be recalled, is fantastic. In the cortex of the posterior portion of the first (and possibly the second) temporal convolution there probably exists a projection zone for fibers of the acusticus for that part of the tonal scale which has to do with verbal sounds. Its destruction may produce pure word deafness, that is to say, deafness without disturbance of internal speech. The perception of word sounds must be bilateral, but only on one side have the intimate functional relations between auditory and motor zones of speech been established. This connection, which is formed essentially by the fasciculus arcuatus is what remains in transcentral aphasias and permits the echolalic language.

For the symbolic understanding of speech and its spontaneous evocation many other pathways have developed in man; from their origin in the sensorial zones they go to the frontal lobes in which they establish connections with other association systems of a prevalently psychic nature; in this way speech is provided with its highest and most varied form of expression.

Through the prefrontal path, those stimuli, which are not memories of words but the order, so to speak, of movements necessary for articulation, reach the operculum rolandi, the real origin of the nerves for motor speech. Through the sensorial path, that indefinable something of time and space, which represents the taxic, coordinator or praxic element of speech, reaches the operculum. In this way the conception of a center of Broca, in which are deposited motor images of verbal articulation, falls by itself.

No longer are there centers of understanding and autonomous centers of speech emission, but instead reflex arcs which become more and more complex in philogenetic and ontogenetic evolution. The attempt to find wider reflex arcs concerned in the phenomenon of speech is justifiable today, when clinical experience and pathologic anatomy prove the existence of more complicated pathways and provide the means for identifying them. Not only the fasciculus arcuatus, but also the longer sagittal pathways of the left hemisphere, the occipitofrontal tract, is concerned with speech. It functions in some way in the comprehension and evocation of speech, and constitutes one of the more complicated reflex arcs (Henschen's Kreise) that establish even wider relations with the remainder portions of the brain.

The known zone of speech must be extended from the occipital lobe to the left prefrontal lobe, especially in its lowest part (F_3 and O_3), exclusive of the insula, the retro-insular subinsular tracts, and the basal nuclei.

Compensation in aphasic disturbances is effected by means of fibers that unite the acoustic center of one side with the motor center of the opposite side, all of which pass into the centrum ovale overhanging the left lenticular nucleus.

NACCARATI, New York.

THE LOCAL MANIFESTATIONS OF COCAIN SNUFFING. G. BONVICINI, Jahrb. f. Psychiat. u. Neurol. **44**:1, 1925.

The cocain habit, according to Bonvicini, began forty years ago; the drug was then taken hypodermically, but for the last thirteen years it has been taken by "snuffing"; this is considered a more "elegant" way of taking the poison, and America is blamed by the author "for presenting this gift" to the world. Owing to the greater convenience of using the drug by this method, the habit seems to be increasing. In previous years cocain was usually taken in combination with morphin, except by persons who acquired the habit as a result of taking the drug for the treatment of chronic nasopharyngeal diseases. Insane asylums and prisons are more often the "terminal landing places" for those using cocain than for those using any of the other habit-forming drugs. As a result of the almost prohibitive price of the drug in Austria, most of the "cocain fiends" in that country come under medical observation in private rather than in public institutions. As the symptoms of the sudden withdrawal of cocain are not as striking and as apparent as those following the sudden withdrawal of morphin or alcohol, any information concerning this phase of the problem must necessarily be obtained only from subjective data.

The first local manifestation of the use of the drug by snuffing or by spraying is a sensation that air is entering the nostrils much more freely than usually; this is accompanied by a feeling of chilliness of the nose and the adjacent skin of the cheek (butter-fly distribution), the tongue, the skin over the glabella and in the region of the upper middle incisors. This peculiar subjective sensation is associated with an objective anesthesia of these parts, as well as of the nasal septum, the anterior portion of the nasal cartilages, the palatal arch and of the pharynx. At the same time there is a diminution in the sense of taste and smell and a disappearance of the nasal and pharyngeal reflexes. After this the patients begin to complain of tightness in the throat, dryness of the lips and buccal mucous membrane and of great thirst. Owing to the anesthesia of the tongue there is great difficulty in moving this organ, and speech becomes thick and indistinct. Later the conjunctivae become pale and "enamel-like," the iris assumes a dark green luster; the pupils are dilated, although they still react to epinephrin and atropin as well as to light and in accommodation, but their reaction to painful stimuli is either diminished or entirely absent.

In advanced cases amblyopia and diplopia are occasionally noted associated with a rapidly disappearing staring gaze which compels the patient on looking at an object to turn his head instead of his eyes. At the same time, owing to irritation of the sympathetic, the palpebral fissures are dilated, the eyeballs become prominent, and these with diminution of nictitation, give rise to a picture not unlike that observed in exophthalmic goiter. The face becomes a waxen hue; this is especially well marked over the back of the nose and over the center of the forehead. When the patient is not under the influence of the drug, he presents a picture which is the direct opposite of that described. The pupils become miotic, the conjunctivae strongly injected, the gaze dull and the back of the nose assumes a reddish and occasionally a bluish color; the nose begins to discharge profusely, the tongue becomes moist again, and the secretion of saliva is increased.

The most characteristic objective signs of the prolonged use of cocain by snuffing are the changes in the nose; these are pathognomonic of the condition. The nose becomes diffusely swollen; its skin assumes a dirty, pale bluish discoloration with a peculiar dull luster which reminds one of the artificial

"gelatin or moulage nose." The shape of the nose is also changed; its tip appears padded and knoblike, and the alae nasi become somewhat swollen, "nez culotté." The nostrils appear unusually dilated with a rose-colored line at their margin, the so-called "nez épaté" or "nez tamponné." Occasionally the margin of skin is covered with a patch of eczema. Characteristic as these changes are, they are not as diagnostic as the intranasal manifestations. Here one finds on the vibrissae in the vestibulum nasi, in the recessus nasopalatinus, in Kiesselbach's area, and more rarely on the lateral walls and lower nasal cartilages, layers of undissolved dirty greenish crystals of cocain, frequently discolored by old blood and covered with crusts. Especially characteristic and diagnostically important are the ulcerations on the mucosa of the cartilaginous septum; in many cases these lead to perforation. Clinically as well as anatomically these ulcerations may be included in the category of the usual "ulcus septi nasi perforans" (Hajek); they also resemble the nasal ulcerations observed in persons engaged in certain industrial occupations.

The author next discusses in great detail, with extensive quotations from the literature, the vascular, neurotrophic, chemical, mechanical and mycotic factors involved in the productions of these as well as of other similar intranasal ulcerations. He lays particular stress on the effect that these factors have on the constitutional defect caused by the excessive use of cocain. He also emphasizes the fact that while the most deleterious effects of cocain snuffing are seen in the tissues that derive their sensory innervation from the trigeminus, the motor phenomena are less serious and less frequent. The latter are chiefly irritative in nature; they consist of a twitching of the masseters and pterygoids which gives rise to the well-known cocain trismus, and later to the risus sardonicus with the usual gnashing of the teeth or clonic movements of the lower jaw. When motor disturbances occur, they usually do not appear until after the sensory symptoms have persisted for a long period; they are never as extensive nor as complete as the sensory manifestations.

The acne, so commonly seen on the nose and forehead of those using cocain, is due not only to the trophic nerve disturbances but also to the general cachexia. In doubtful cases the acne becomes of diagnostic importance, because when the use of alcohol can be excluded, the rash disappears promptly with the cessation of cocain snuffing, to reappear just as promptly with the renewal of the habit.

Although most of the symptoms are referable to the trigeminus, the other cranial nerves are not immune from involvement. Olfactory disturbances may occur in the form of anosmia, parosmia and kakosmia (smelling as if something were burning). Motor symptoms are also rarely observed in the distribution of the facial nerve; some of the patients are unable to move the lower part of the face, or, owing to weakness of the corrugator muscles, they are unable to wrinkle the forehead, or there is a disturbance in the mimetic movements of the entire facial musculature. The peculiar laughter of the chronic cocain snuffer is not only well known to the "fiends" themselves, but also to the producers of moving picture films. Bonvicini states that although he himself has never seen a case which presented facial tic or tremors of the lips, other observers have reported cases not unlike those occurring in "rire en traves" seen in bulbar paralysis, parkinsonism and encephalitis. Cases have also been reported with constricted visual fields, especially for colors, photophobia, slight pallor of the nerve heads, narrowing of the retinal vessels, diplopia and other signs and symptoms suggestive of disturbances in the oculomotor system.

KESCHNER, New York.

EXPERIMENTAL CONTRIBUTION TO THE STUDY OF THE NORMAL SUBSTANTIA NIGRA AND OF ITS RELATIONSHIP TO THE CEREBRAL CORTEX AND THE CORPUS STRIATUM. A. FERRARO, Arch. gen. d. Neurol., Psich. e Psichoan. **6**:26-117 (March) 1925.

In this work, conducted under the direction of Professor Winkler, the author has made a valuable contribution to the solution of some important problems inherent to the relationship of the substantia nigra to other parts of the brain, especially to the extrapyramidal system.

An historical review of the anatomy, physiology and pathology of the substantia nigra, beginning with the early works of Vicq D' Azyr and Soemmering, opens the article, and is followed by a clear description of the normal substantia nigra in cat, dog and rabbit, on which animals the researches were conducted. The experiments are divided into three groups: First, animals in which the cortex was partially or extensively extirpated while the corpus striatum was left intact. Second, partial or total extirpation of the pallium and partial destruction of the striatum. Third, animals in which the partial or total extirpation of the pallium was accompanied by marked or total destruction of the striatum. The sections were stained with thionin and differentiated with Gottard's Fluid.

The general conclusions reached by the author are: The normal substantia nigra is derived, partially at least in the caudal regions, from the formatio reticulata, from a posterior group of cells which is closely connected with a more frontal medial group. This derivation, generically suspected by others, is confirmed and clearly illustrated in the author's cases, especially in the cat.

The substantia nigra of the dog, cat, and rabbit, even though it is connected with the cortex through the radiation by way of the pes pedunculi, cannot be considered as dependent on the cortex in the same way that the optic thalamus is; its cells do not disappear as a result of cortical extirpation. After extirpation of the cortex there is a global reduction of the volume of the substantia nigra, owing to the degeneration of the underlying pes pedunculi which is due to degeneration of the intercellular molecular layer, and to the volumetric diminution of the nerve cells. The greater number of the substantia nigra cells are preserved after extirpation limited to the area frontalis, centralis and parietalis, as well as after extirpation of almost all the neopallium. From these facts it must be concluded that in the interrelations between the cortex and the substantia nigra, a system of fibers originates from the cortex which, partially at least, goes to the cells of the substantia nigra. Fibers passing in the opposite direction, from the substantia nigra to the cortex, must be scarce, if they exist at all.

Disappearance of the larger number of the nerve cells of the substantia nigra follows almost complete destruction of the striate body. This disappearance does not assume systemic characteristics and the cells that remain are markedly reduced in volume, while the intercellular molecular substance appears far more degenerated than it does after a simple cortical extirpation. It appears, therefore, that the axons of the substantia nigra cells converge for the most part on the striate body, constituting relations of utmost importance; certainly, these are the most numerous connections that the substantia nigra establishes with other parts of the encephalon. The concept of a prevalent dependence of the substantia nigra on the cerebral cortex must be abandoned and be replaced by that of a prevalent dependence on the striate body.

After extirpation of the cortex in toto and of all the striate body, especially in the rabbit, a certain number of cells remain which, although reduced in

volume, have some normal characteristics. These cells are found especially in the frontal planes and more particularly in the dorsomedial region. Such cells, therefore, do not seem to depend on the striatum and may establish relationship with other parts of the encephalon, such as the thalamus, as Besta claims, or they may constitute the origin of the peduncular pathways (Mingazzini, Foix, Wiener and Münzer, etc.), or of the tegmental pathways, whose origin is still a matter of discussion.

NACCARATI, New York.

MALARIAL TREATMENT OF MULTIPLE SCLEROSIS. Karl Grosz, Jahrb. f. Psychiat. u. Neurol. **43**:198, 1925.

Forty-two patients with multiple sclerosis were treated with malaria at the University Clinic in Vienna between 1921 and 1923. In nine of these cases the malarial treatment was combined with the administration of typhoid vaccine, the latter either preceding or following the former. At the end of the treatment each patient received neo-arsphenamin (a total quantity of 3.15 gm.). The blood was taken from a donor who was free from syphilis and usually, though not always, during the height of a tertian paroxysm. No more than 4 c.c. was ever used. One injection seemed sufficient in almost every case. If no reaction set in after the usual period of incubation (about ten days), a provocative 10 per cent. injection of solution of sodium nucleinate (5 c.c.) was given intramuscularly. As a rule, the patients were allowed to have from eight to ten paroxysms. The highest temperature observed was above 41 C. (105.8 F.) after which the quinin-neo-arsphenamin treatment was begun, as in general paralysis. There were no severe complications.

Of the forty-two patients treated, only eleven (26.2 per cent.) showed definite improvement; of these, five gave a history of previous remissions, two had acute and four chronic and progressing cases. Among these eleven cases there was definite improvement in the cerebellar gait in six; in two there was definite improvement in audition; in two, improvement in the spastic paresis of the upper extremities; in one acute case with nystagmus, hemiataxia, hemiparesis, cerebellar gait, Romberg and pyramidal tract signs, only the nystagmus and slight hemiataxia remained.

In eighteen cases (ten progressive, six remitting, two acute), i. e., 43 per cent. of all cases, the improvement was much less marked; in five of these the paresthesias, headache, backache and sensation of choking disappeared; in six, the cerebellar gait was much improved.

The author emphasizes the importance of bearing in mind that remissions generally occur in this disease in attempting to attribute favorable results to any form of treatment employed. He also points out that although the results of malarial therapy are not as good in multiple sclerosis as in general paralysis, nevertheless there is sufficient justification for the further use of malarial treatment in the former. As all patients were treated with malaria and neo-arsphenamin, no conclusions can be drawn as to the effects of the latter in the treatment of multiple sclerosis.

In nine cases, typhoid vaccine was employed in addition to malaria; in two of these, good results were obtained from typhoid vaccine as well as from malaria—these were chronic remittent cases; two showed slight improvement; one did not react to typhoid but reacted to malaria; in two cases with considerable improvement following malaria, the intravenous injection of typhoid vaccine was followed by still better results; in two cases, neither typhoid nor malaria had any effect. The author, therefore, is unable to draw any conclusions from this group of cases.

Catamnestic investigations for a period of two years showed that the results obtained, even the slight improvements, were more or less permanent. A comparison of the cases treated with staphylococcus vaccine and reported on by the author in a previous communication, with the cases treated with typhoid vaccine and malaria, would seem to show that the results with typhoid vaccine were superior to those obtained with staphylococcus vaccine, whereas the results following malaria were not as satisfactory as those following treatment with either of the other two.

KESCHNER, New York.

THE MENINGEAL TUMORS: A CRITICAL REVIEW. ROUSSY AND CORNIL, Ann. d'anat. path. med.-chir. **2**:63, 1925.

Although nothing much has been added to the gross description of the meningeal tumors since the time of Virchow, it is far otherwise as concerns their histology. At present even the question of their origin is being warmly debated. Originally it was sufficient to call them psammomas on account of their calcareous concretions. Later they were named endotheliomas from the tissue from which they were supposed to spring, and only recently Cushing has swung away from the endothelial theory and given these tumors a place of their own by calling them the meningiomas. Oberling has recently brought new light to bear on this question and comes out forcibly in favor of the ectodermic origin of these meningeal tumors. They are apparently always inseparably connected with the dura, although they may often be shelled out from the surrounding brain tissue without even the most minute destruction of the cerebral substance. They frequently extend into the bone and produce hyperplastic changes which may be recognized roentgenographically.

Histologically, there are three main types: the neuro-epithelial with bizarre nuclei and nucleoli; the fusiform neuroglial, the most frequent type, with its whorls and resemblance to the peripheral gliomas springing from the nerves; the connective tissue (fibromatous or sarcomatous) tumors, which resemble those springing from subcutaneous tissue, and which usually arise from the dura. Calcareous granules may be found in any type. The authors conclude from an extensive study that these chalk bodies arise as buds from vessels which undergo calcareous degeneration, as intravascular projections which first become hyalinized and later calcified, or from the tumor cells which elaborate a collagenous substance that is later infiltrated with lime salts.

Recent departures which classify the meningiomas with the epitheliomas are based on the development of the cerebral membranes and the histologic character of the tumors. Instead of three membranes there are only two, the dura, and two or more layers of pia. The pia is projected along the nerves, forming their sheaths. Cushing objected to the name endothelioma because these tumors arise from the pia (or its superficial layer, the arachnoid), and involve the dura secondarily. Consequently, he coined the term meningioma. According to Oberling, the leptomeninges are formed from meningoblasts arranged in an extensive syncytium extending between the nervous parenchyma and the dura. These meningoblasts originate from the neuroglia, and arise from the neural tube. Several minor reasons are given for this statement: the homology of the leptomeninges with the sheath of Schwann, the presence of melanoblasts in the pia, the variety of tumors arising from the meninges, Recklinghausen's disease and, finally, the rare but important diffuse gliomatosis of the pia.

Roussy and Cornil, therefore, concur with the opinion of Oberling that tumors of the meninges are ectodermic in origin, although a few may arise from the dura, that is the mesoderm.

FREEMAN, Washington, D. C.

THE PHYSIOLOGY OF THE DESCENDING SPINAL TRACTS. THE PATHWAYS FOR THE "NECK REFLEXES." E. A. SPIEGEL and DONALD J. MACPHERSON, Arb. a. d. neurol. Inst. Wien. Univers. **27**:189 (May) 1925.

It is generally assumed that the long descending tracts from the cortex and subcortical ganglia subserve the transmission of reflexes from the oral to the caudal segments of the body, i. e., that they mediate reflexes which have their receptive area in the region of the head, neck and partly also in the fore limbs, whereas the reflexes for the lower segments are mediated by shorter tracts whose site of origin is within the spinal cord itself. Various investigations of the physiology of such reflexes, as the "trotting reflex," the "scratch reflex," the "trunk shaking reflex" etc., have been published by Luchsinger, Haycraft, Goltz, Ewald, Sherrington, Laslett and others. The present paper is devoted to the study of the more recently described neck reflexes, the so-called "Magnus-de Kleijn reflexes." These reflexes consist of a change in tonus of the extremities following changes in the position of the head in its relation to the trunk. They can be best studied in decerebrated animals after the removal of both labyrinths in order to eliminate the effects of the labyrinthine reflexes. Under these conditions it has been found that during dorsal flexion of the head (elevating the head) there is an increase of extensor tonus in the fore limbs with a diminution of tonus in the hind limbs, whereas during ventral flexion of the head there is a diminution of extensor tonus in the fore limbs with an increase of tonus in the hind limbs. On rotating the head to the right, there is an increase of extensor tonus in the right fore and hind limbs with a diminution of tonus in the left fore and hind limbs. On rotating the head to the right around a sagittal axis, so that the vertex is directed to the right and the chin to the left of the animal, there is a diminution of extensor tonus in the limbs on the right side, with an increase of tonus in the limbs of the left. According to Magnus and de Kleijn the afferent pathway of these reflexes in the cat run in the three upper cervical posterior roots, the centers for them being in the first two cervical segments. The object of this study was to determine the intraspinal course of this reflex pathway between the uppermost cervical segments and the spinal centers for the extremities. As all parts of the cord, the anterior, lateral and posterior columns, contain descending systems, the problem was to ascertain which of these bundles of fibers could be sectioned without disturbing the neck reflexes, and which level had to be preserved in order to enable one to elicit them. Ten cats were decerebrated, and various longitudinal and transverse sections were made. As a result of their experiments these authors conclude that the intraspinal component of the neck reflex is not to be found in the posterior nor in the anterior columns. It seems that the descending tracts which mediate the neck reflexes run their course from the uppermost cervical segments in the corresponding homolateral lateral column. They are in close relationship with the other tonus regulating systems in this column, but seem to be located preponderatingly in the most dorsal portion of the lateral column.

KESCHNER, New York.

THE RELATION OF NERVES TO DEGENERATING AND REGENERATING TASTE BUDS. R. M. MAY, J. Exper. Zool. **42**:371 (Oct. 5) 1925.

An examination of the taste buds in the catfish *Ameiurus nebulosus* (Lesueur) reveals that their innervation is composed of unmedullated neurofibrils. In all cases there is contiguity, and not continuity, between the nerves and the taste cells. All gradations in form are found between so-called sense cells and so-called sustentacular cells. This confirms the belief in a single type of gustatory cell. The nerve arborizations to the taste buds degenerate and disappear within a few hours after section of the nerve trunk. The nerve fibers within the distal stump of the cut nerve begin to degenerate several days after the nerve terminations have completely disappeared. Degeneration is thus centripetal. The cells remain intact for several days after their nerve arborizations have disappeared. At 20 C., the degeneration of the taste cells occurs at the height of degeneration within the nerve trunk. At such a temperature there is a synchronous degeneration of medullated sheaths and axons within the nerve.

Regeneration of the nerve begins at a time when parts of it are still in the process of degeneration. Regeneration of the taste cells is brought about when the regenerated neurofibrils enter the places where taste buds had formerly existed. The evidence indicates that the taste cells regenerate under the influence exerted by the newly formed nerve arborizations. It is the ordinary epithelial cells that differentiate into taste cells. There is no evidence to show that the outgrowing nerve endings are led by attracting substances, from undegenerated elements, to their place of termination. The taste cells, during their regeneration, are never found in continuity with the neurofibrils. The regenerated nerve arborizations are first formed of fewer neurofibrils than are found in normal taste buds. After a few days the normal number of neurofibrils is again seen in the regenerated taste buds.

At a temperature of about 13 C. the medullated sheaths within the distal cut end of the nerve disintegrate slowly, but the axons within this stump show no evidence of disintegration. At such a temperature the taste buds degenerate somewhat more slowly than they do at 20 C. At such a temperature the taste buds regenerate very slowly, after the axons have healed by first intention. After the nerve trunk is healed and the taste buds have regenerated, a temperature of 24 C. causes no further change.

The evidence at hand is interpreted to mean that some substance, of the nature of a hormone, is continually being given out by the nerves to the taste cells. This causes the taste buds to retain their normal status. The absence of this substance is enough to cause the disintegration of the taste buds, although the axons within the nerve do not degenerate.

WYMAN, Boston.

LANDRY'S PARALYSIS WITH FINDINGS OF ACUTE ANTERIOR POLIOMYELITIS. MONA ADOLF, Jahrb. f. Psychiat. u. Neurol. **43**:40, 1924.

CASE 1.—A previously healthy man suddenly became ill with pains and weakness in one leg; the next day both legs became paralyzed. Within a few hours after admission to the hospital, the paralysis rapidly ascended to the trunk and upper extremities; simultaneously with the progression of the paralysis he developed severe dyspnea, to which he succumbed. On histologic examination the brain and cord showed marked involvement of the vessels; the perivascular lesions and the intense destruction of the ganglion cells with

the existing neuronophagia were identical with the histologic picture usually observed in poliomyelitis. Bacteriologic examination was negative. As careful investigation revealed no relationship (I presume the author means, no *etiologic* relationship) to infantile spinal paralysis, the case is diagnosed as acute anterior poliomyelitis adultorum with a Landry syndrome.

Case 2.—A man, aged 24, became ill on Nov. 23, 1919, with general prostration and drawing pains in the joints. After staying in bed for a few hours he found that he was unable to move both lower extremities; there were no objective sensory disturbances. On the following day he was unable to sit up in bed, and his neck became rigid. On November 25, he was hardly able to move his upper extremities; his sphincters remained intact. On November 26, he developed severe dyspnea, for which he was removed to the hospital. Examination showed normal cranial nerves (in view of the reported dyspnea, I doubt the correctness of this observation), absent reflexes (not mentioned whether deep, or superficial, or both); no Babinski sign, positive Kernig sign; slight movement of the upper extremities, complete paralysis of the lower, except for slight ability to move the toes; there were no sensory and no sphincteric disturbances. The patient was extremely pale; his lips and nose were cyanotic. (There is no report of spinal fluid findings in this case nor in Case 1.) The weakness and paralysis were steadily increasing, and death occurred on Nov. 30, 1919. Necropsy showed evidences of a hemorrhagic encephalitis and myelitis. Sections of almost all levels of the cord and brain stem showed the histologic picture of poliomyelitis. The meningeal infiltration and hyperemia were much more extensive than in Case 1; there were many hemorrhages throughout the cord, especially in the lumbar enlargement, and marked destruction of ganglion cells. In the region of the aqueduct of Sylvius there were many distended capillaries and small-cell, perivascular infiltrations, but no such hemorrhages as are usually found in Wernicke's superior hemorrhagic encephalitis. The cord also showed glial changes. The differences in the histologic pictures in the two cases is attributed by the author to the differences in the duration of the illness, the latter being much longer in Case 2 than in Case 1.

Keschner, New York.

On the Effects of Radiothery in Tumors of the Central Nervous System. G. Artom and M. Bolaffio, Riv. Oto-neuro-oftal. **1**:43 (March-June) 1924.

The authors present two cases of cord tumor and thirteen cases of brain tumor of varying localization and nature which were submitted to roentgenotherapy. Except in a few instances when the maximal dose with short intervals was given, applications consisted of a half dose each time, three half doses in all, with intervals of seven days. Among the phenomena observed immediately after the irradiations, the authors report one death (gumma of the right temporal lobe in a patient who received a full dose), and the usual symptoms of headache, vomiting, tachycardia and tachypnea. They observed also slight hyperthermia in a few cases, hiccough in one case, herpes zoster in one case and psychic symptoms in a little girl.

The results obtained in the two cases of cord tumor (glioma and gliosis) seem to indicate that there was some remission and retardation of the course; two cases, however, are too few to warrant definite conclusions. Regarding the brain tumors, the authors state that roentgen irradiations are useful in cases of pituitary tumor with acromegaly. Retardation of the course, remission and improvement of the headache, the hypersomnia, the asthenia of vision and of the sexual disorders may be obtained. In cases of extrapituitary tumors, the

roentgen irradiations cannot modify the outcome of the disease, but in many cases they produce improvement of the general symptoms, especially of the headache and vomiting. The influence on local symptoms is less evident, and is essentially limited to the cerebellar symptoms. Roentgen therapy is consequently indicated for patients with severe headache and vomiting, and for those presenting preeminently cerebellar symptoms.

The authors then discuss the choice between radiotherapy and other therapeutic procedures (decompression, extirpation of the tumor, etc.); they conclude that the inaccessibility of many tumors and the poor results from surgery still demand the use of palliative measures. Important considerations militate against decompression and in favor of radiotherapy in many cases; this method should be tried not only in cases in which the tumor is inoperable, but also in those that are operable. There is only one exception, the cortical or immediately subcortical tumors of the rolandic zone; these tumors present the most favorable conditions for radical treatment and the most unfavorable conditions for radiotherapy.

NACCARATI, New York.

THE COMPARATIVE ANATOMY OF THE NUCLEUS VESTIBULARIS TRIANGULARIS. 1. NUCLEUS INTERCALATUS AND NUCLEUS PREPOSITUS HYPOGLOSSI. JUNGORO TAKAGI, Arb. a. d. Neurol. Inst. Wien. Univers. **27**:157 (May) 1925.

At the caudal end of the medulla there is to be seen a collection of small cells between the hypoglossal and dorsal vagus nuclei; this collection of cells has been designated as the nucleus intercalatus (Staderini). Oralward to the hypoglossal nucleus this nucleus joins a rounded nuclear mass; this mass is apparently an independent structure, separated from the anterior portion of the vagus nucleus and from the mesially placed nucleus triangularis. Marburg has designated this mass of cells the nucleus prepositus hypoglossi.

Serial sections of the medulla of various animals (rats, guinea-pigs) were carefully examined by Takagi, and he concludes that this nucleus is an independent structure and has no anatomic connection with the nucleus intercalatus. In contrast to the latter, it consists of two different elements: large cells analogous in structure to motor cells, and small cells. There is no doubt that the large cells are not a coincidental finding, because they were found in all animals examined, and Marburg was also able to demonstrate them in man. They have nothing to do with the hypoglossus but are probably related to the large cells in the formatio reticularis. As far as the small cells are concerned, the general opinion has hitherto been that these belong to the cells of the nucleus vestibularis triangularis, but this, according to Takagi, also needs revision. Because the nucleus in question is contiguous to the triangular vestibular nucleus and also to the vagus at its caudal surface, one is not justified in assuming that it has only one connection, but that it is connected with two sensory (sympathetic) nuclei and with one nucleus whose motor character cannot be questioned. With this anatomic conception in mind, it would seem that the connection of this nucleus with the vagus nucleus on the one hand and with the vestibular nucleus on the other is predestined to have some functional property which is simultaneously influenced by both nerves derived from the aforementioned nuclei. This function is the regurgitation of foods. Takagi believes that his theory concerning this nucleus finds corroboration in Spitzer's view that the function of the triangular nucleus, so far as the metabolism of nutrition is concerned, is related to its connection with the sympathetic nucleus, and also in Jacobson's view that the function of the dorsal vagus nucleus is only sympathetic in nature.

KESCHNER, New York.

THE REACTION OF THE LARVAE OF VANESSA ANTIOPA LINN. TO SOUNDS. D. E. MINNICH, J. Exper. Zool. **42**:443 (Oct. 5) 1925.

The larval instars of the mourning-cloak butterfly, *Vanessa antiopa* Linn., respond to appropriate sound stimuli by throwing the anterior third of the body dorsad or dorsolaterad. The responsiveness to sounds increases greatly with age, being least in the first and greatest in the last two instars (fourth and fifth). The larvae respond to the various forms of mechanical stimulation in all instars. The responsiveness to the ordinary forms of mechanical stimulation decreases greatly with age, being greatest in the first and least in the last instar. Decapitated bodies and fragments of bodies will respond to sounds, showing that the sense organs concerned in this response are widely distributed and that the response is more or less segmental in nature. Certain of the hairs located chiefly in the anterior two thirds of the body in all probability constitute the organs of sound reception.

The extent of the response to a tone varies with the intensity of the tone. For full-grown larvae the upper threshold of response to tones is probably not far from C^2, 1,024 vibrations per second. Responses were obtained from 1,024 to 32 vibrations per second, the lowest frequency tried. Larvae subjected to a tone stimulus of short duration repeated at intervals of five seconds show little or no fatigue in the course of a hundred trials. Larvae subjected to continuous tone stimulation generally become fatigued and cease to respond after a period of from five to sixty seconds. This is due, in general, to one form of stimulation inhibiting the response to another form of stimulation. When the air current is long continued, however, another factor, probably that of fatigue, also enters in. When fatigued to C, 256 vibrations per second, or G, 384 vibrations per second, larvae do not respond to C^1, 512 vibrations per second. When fatigued to C^1, however, they still give 100 per cent. response to C, and about 50 per cent. response to G. These results are tentatively explained on the basis of the extent to which hairs of different dimensions are affected by the various pitches in question.

WYMAN, Boston.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

The Four Hundred and Twenty-Second Regular Meeting, Oct. 6, 1925

I. Abrahamson, M.D., *President, in the Chair*

An Unusual and Protracted Case of Schilder's Disease. Dr. Walter M. Kraus and Dr. Arthur Weil (by invitation).

A small number of cases of diffuse brain sclerosis have been reported. In 1912, Schilder selected a few and, adding two of his own, defined a disease which he called encephalitis periaxialis diffusa and believed to be a clinical and pathologic entity. Many different names have been used to characterize the disease, indicating the divergence of opinion regarding its characteristics and the variations which may occur. We find encephalitis periaxialis diffusa, chronic diffuse encephalomyelomalacia, *sclérose intracérébrale centralobaire et symmétrique;* or a more general classification under diffuse sclerosis. The list of cases accepted as this form of diffuse sclerosis is different in each paper on the subject.

The cases reported, in general, give the impression of a toxemia which spreads through the central nervous system. The distribution is diffuse, often comprising the subcortical region of a whole hemisphere. In the spinal cord it may extend from the cervical to the lumbar regions. The disease is not restricted to any particular decade of life. Most of the patients die between the ages of 20 and 45. Both children and adults have been affected. The duration of the disease is from a number of weeks to fifty-two years.

The case to be reported is that of a Russian Hebrew tailor, born in 1877, whose family and past history were unimportant. In 1911, while walking in the street, the patient suddenly fell to the ground helpless and could not get to his feet again without assistance. There were no convulsions and no loss of consciousness. Sensory disturbances, ataxia, pain and anesthesia to touch, were noticed in all four extremities, but disappeared after a few weeks. The cranial nerves were normal with the exception of slight deviation of the protruded tongue to the right. In December, 1911, there was slight concentric contraction of the visual fields. At this time he also showed: diminished sense of smell; a slight tremor of both hands; ankle clonus which was inexhaustible on the right, exhaustible on the left; inexhaustible knee clonus on both sides; the upper abdominal reflexes were present, the lower were absent on the left; a pseudo-Babinski sign on the right and markedly exaggerated knee jerks; no ataxia; occasional incontinence of urine.

This condition remained nearly unchanged for five years when the patient was discharged from Montefiore Hospital. After another five years, in 1921, the same neurologic status was revealed, with an increase of the eye disturbances, insufficient convergence of the right eye, weakness of the rectus internus and externus on both sides, irregular pupils with reaction to light, but none in accommodation. The right arm was weaker than the left and the biceps and triceps reflexes were lively on both sides. There was slight ataxia

in the left arm, marked ataxia on the right, and ataxia of both lower extremities with loss of sense of position of the toes. A marked Romberg sign was present. There were no sensory changes. The gait was peculiar; it required a cane and was characterized by small steps with shuffling of the feet. Every time the foot touched the floor there was hypertension at the knee. Speech was very rapid and scanning, with a peculiar repetition of the last word of each sentence. This condition was progressive, and in July, 1923, the patient could not stand or walk. There was a mild degree of dementia.

In March, 1924, complete left hemianesthesia was noted. In June, 1924, the patient died after an acute attack producing left-sided convulsions and anesthesia. We wish to emphasize the onset with spinal symptoms, the remissions and the great variety of signs and symptoms.

In the histologic examination of the central nervous system the most striking finding was the great extent and localization of demyelinization. In gross sections of the whole brain stained for myelin sheaths, demyelinization involved all lobes and the corpus callosum. Most of the arcuate fibers were intact and dark colored, forming a striking contrast to the pale color of the underlying demyelinated area. Similar areas of demyelinization were present in the basal ganglia, cerebellum and pons. The patches of demyelinization were very clearly separated from the unaffected nerve tissue. In the spinal cord, the transition between demyelinated and intact areas was more diffuse. Definite tracts were not affected, the area of degeneration involving the pyramidal tracts as well as the extrapyramidal and marginal tracts and varying from segment to segment. The posterior columns were almost unaffected. Wherever examined, the destruction of the axis cylinders was not parallel to the demyelinization. With specific axis cylinder stains, it was found that in a given area the number of axons was greater than the number of myelin sheaths, but most of the remaining axis cylinders showed signs of swelling. The anterior horn cells in the segments of demyelinization showed in some instances signs of beginning degeneration, swelling, disappearance of Nissl bodies, fine granulation and vacuolization. No conspicuous cell changes were noted in the brain. In the brain, where destruction of the myelin sheaths occurred, marked increase of glia tissue was noticed. The scar formation was marked in the subcortical region. The blood vessels showed a perivascular infiltration with marked vacuolization of the surrounding tissue and great dilatation of perivascular lymph spaces. Perivascular small cell infiltration was noticed especially in the region of the corpus striatum and was combined with small hemorrhages. Throughout the brain, accompanying the blood vessels, large amounts of amyloid were found in the form of small globules which were closely packed in the subarachnoid region and around the ependymal layer of the ventricles. Fat stains revealed numerous cells laden with small fat drops in the outer layers of the cortex and the pia.

The meninges showed no signs of acute inflammation and were intact except for slight edema with thickening of the pia arachnoid over the convexities of the brain.

If we summarize this histologic examination, we find a markedly diffuse demyelinization with new formation of glia tissue, and a perivascular reaction. This picture, both in the brain and in the spinal cord, was distinctly different from that of multiple sclerosis, not only in type, but also by the manner of its extension and diffusion. The histologic picture seems to justify the claim that this disease is a pathologic entity.

DISCUSSION

DR. J. RAMSAY HUNT: I recall examining this patient a number of years ago with the late Dr. Joseph Fraenkel. I remember that we were puzzled by the clinical picture, which presented both cerebral and spinal features. Multiple sclerosis was considered, but we were more inclined to think of a cerebrospinal arteriosclerosis, largely because of the very characteristic *marche à petit pas*. During the years in which I was especially interested in pathologic anatomy, I was on the outlook for cases of diffuse lobar sclerosis, so called, but never encountered them. I wish to ask Dr. Kraus if the axis cylinders were involved in the sclerotic areas in his case, or whether they showed that preservation in the old sclerotic areas which is so characteristic of the pathologic lesions of multiple sclerosis. This brings up the interesting question as to the possible relationship of this disorder to some cases which have been hitherto regarded as belonging to multiple sclerosis.

DR. ABRAHAMSON: The patient was under my observation during his entire stay in the Montefiore Hospital. During the first period, he presented the peculiar gait of rapid, short, side to side steps, a repeated stammer in speech, an inexhaustible ankle clonus on both sides, but without a definite or constant Babinski sign; he flushed very easily, especially on observation or on being asked to exhibit his gait. The marked suggestibility made the diagnosis of hysteria occur to some of the observers, but most of us felt we were dealing with a condition that had evidences of organic disease. The gait on closer examination differed markedly from that seen in dysbasia arteriosclerotica; there were no evidences of arterial disease. On his second admission to the hospital, the signs and symptoms were markedly accentuated, and new and definite signs were to be found indicating that the condition was undoubtedly organic. At that time I noted in the hospital records that he presented a syndrome not known to me by experience or by reading. I called it a new disease and owing to the fact that certain features, as the tremors, the gait, and the speech, had been observed in postencephalitic basal ganglion disease, I predicated that the site of the morbid process was most likely in the basal ganglia. This condition became rapidly worse, and it was soon evident that we were dealing with a diffuse and widespread disease which also affected the basal ganglia. The diagnosis of Schilder's disease was made postmortem on the pathologic findings.

DR. JOSEPH GLOBUS: The diagnosis I have made, and later verified by anatomic study, in the case referred to by Dr. Abrahamson, was "diffuse subcortical encephalopathy" and not "Schilder's disease." I do not believe that Schilder himself would so dignify a disease picture which lacks uniformity of the pathologic process as well as of the clinical manifestations. From 1912 to 1924 Schilder reported in all three cases. What characterized these cases? First, a change in the white matter; but this was not limited to one particular area or to a given system of tracts. It was not a strictly systemic disease. No two of the three cases reported were exactly alike in the extent of the involvement of the white matter. Nor is it true that in all the cases the disease was limited to the white matter. From his illustrations and description you will see that he is dealing primarily with a diffuse meningo-encephalitic process; he speaks of meningitis with numerous lymphocytic cells in the subarachnoid space. You will see also cortical involvement with a definite productive inflammatory process in the gray matter. With such a bizzare and disseminated pathologic process little can be said for a definite disease entity;

simply because Schilder has assembled a few unusual forms of encephalitis, it is not necessary to name a disease after him.

In the small number of cases which he put under the name of encephalitis periaxialis diffusa there is fairly definite evidence of an inflammatory process with secondary degenerative changes. He tried to include and group with his cases a number of other encephalopathies in which degenerative features were predominant without being able to suggest a common etiologic factor.

What is there in the clinical picture to establish it as a disease entity? He speaks of blindness which he claims is due to involvement of the occipital lobes; but in two instances papilledema was established, leading to the diagnosis of brain tumor in one instance, with craniotomy and a fatal issue as the result. With such findings is it necessary to call on occipital localization to explain partial or complete blindness? It is also said that mental deterioration is caused by involvement of the frontal lobe and that peculiar changes in the sense of smell occur early in the disease because of changes in the temporal lobe. With the frontal, temporal and occipital lobe involvement, it would appear that there is not much left to become involved by the disease process, and it certainly does not support the belief that such a wide localization is characteristic of the pathologic process in this so-called Schilder's disease.

What is there in the finer histologic picture? Throughout his material there are numerous inflammatory foci. Perivascular infiltrations with plasma cells are common. In all three cases the process is rather acute and progressive.

Recently, a few cases have been described by English observers, but they differ from those described by Schilder in that they present features more of a degenerative form of disease, with little evidence of inflammatory changes.

I think great care should be exercised in attempts to establish the nature of the disease which we are all too ready to name after Schilder, without there having been established such a disease entity. For the time being we should group such cases with the subcortical encephalopathies as disease processes, of as yet unknown origin, primarily involving the white matter.

Dr. Walter M. Kraus: In answer to Dr. Hunt, the axis cylinders were degenerated in some areas, while in others a good many were present. The destruction of axis cylinders has been observed frequently, and apparently makes the present name of the disease, encephalitis periaxialis diffusa inaccurate.

In general, I am quite in sympathy with Dr. Globus' view. With his statement that it should be called a diffuse subcortical encephalopathy, I agree. With reference to his comment about the optic nerve and disk changes, I do not believe that a slight choking is in any way a cause for complete blindness. I may not have understood Dr. Globus, but that is what I thought he said. I do not believe that this could be used as an argument. Only three of the thirty cases showed eyeground changes. The differentiation between inflammatory and degenerative types is a difficult problem, but it has been observed that in some cases the scar tissue overgrowth is very marked and in others very limited, depending largely on the duration of the disease. As to the diversity of symptoms, I should say that a process so generalized would naturally produce diversified symptomatology. I think that the disease can be made into a syndrome; that it always starts in the occipital lobes, however, and travels forward is not correct. To give Greenfield and Collier credit, they state this in the latter part of their article. They have simply attempted to establish a syndrome for the majority of cases.

The problem of classifying this condition is difficult. However, the case reported coincides with those from Greenfield's laboratory and with a number of others. I made the comment at the beginning that there were approximately thirty cases recorded, and I emphasized that the different authors writing on the subject have rejected some and included others as typical cases. I feel that all the men who are in touch with this condition should judge each other's material personally and form some conclusion in that way.

A Case of Pseudo-Heterotopia of the Spinal Cord. Dr. Arthur Weil (by invitation).

The case reported was that of a man, aged 22, who died of tuberculous pneumonia at the Montefiore Hospital. No anatomic lesions of the spinal cord were found during the necropsy, and the meninges were intact. After opening the dural sheaths, a cordlike formation was found at the anterior surface of the cervical segment, which measured from 2 to 4 mm. in diameter, and went down to the upper dorsal segments, where it disappeared gradually in the spinal cord. This formation was in part closely connected with the spinal cord, and in part separated from it by the pia.

In transverse sections at the fourth cervical level a formation was seen at the anterior part of the spinal cord, which resembled a reduced half of the spinal cord, and consisted of gray matter in the form of an anterior horn surrounded by nerve fibers. At first the diagnosis of a duplication was made, but in serial sections it was proved that the small cord, which was without a pia, gradually lost its gray matter and fused with the original cord. It disappeared totally in the midthoracic region, and here its artefact nature was proved by the loss of part of the anterior horn and anterior columns with laceration of the pia. The artificial duplication had been produced during the necropsy by pulling the cord upward and thus separating a part which was glued together with the original spinal cord at a higher level.

A study of the literature of the last three decades reveals that most of the published cases of complete duplication of the spinal cord were instances of artefacts. Among those remaining, no case could be found which could be traced back to a double embryonic anlage. The majority of them were produced by the formation of embryonic fissures, curvatures of the medullary plate or separation of the spinal cord by new formation of the spine, connective tissue overgrowth, or tumors.

The case reported impresses us again with the necessity of proving the artificial character of a duplication by complete serial sections and by demonstrating the presence of a lesion of the meninges or of the spinal cord substance.

The Need of Psychanalytic Clinics and Institutes in America. Dr. L. Pierce Clark.

Progress in the field of neuropsychiatry within the past two decades has been striking; largely within this period we have seen the formation of mental clinics for the study and treatment of nervous disorders as a necessary part of the curriculum of the medical school. Their existence as a separate entity, however, in different cities and communities has been one of the important accomplishments of the National Committee for Mental Hygiene. While these mental clinics have aimed to render medical and social service and help the individual to make conscious adaptations, their function has not met the great problem of the neurotic in whom the unconscious motivations of the disorder must be brought to light.

My suggestion for the founding of psychanalytic clinics or institutes is not unique. Two such clinics have been in existence for several years in Vienna and Berlin. During my visit to the Ninth International Congress of Psychanalysts which met in Homburg in September, I had a long conference with the heads of both these clinics, and I was particularly interested in the development of the one in Berlin. In 1918, Freud stated that the time was not far distant when it would be regarded as an urgent duty of the state to give aid to the soul as to any other life-saving and health-promoting agent, and thus psychanalysis would be made accessible to an increasing circle of peoples in all conditions of life.

The difficulties encountered by Dr. Eitingen and his colleagues in establishing the Polyclinic in Berlin are somewhat similar to those experienced in this country. After the World War they found that neurotic disorders had grown without measure and the confidence of the public in psychanalytic procedure had kept pace with this urgency for relief. Under the stress and misery of the war it seemed that a sort of utopian policy was about to be put into operation, for the government officials apparently were willing to do almost anything to advance the cause of the nervously sick. When the collapse came, however, they not only withdrew their sympathetic support, but actually became hostile to all former promises. In this country, immediately after the armistice, we all know how even the more popular and well established institutions suffered. It is, perhaps, but a natural heritage of war to expect this attitude to follow in economically depleted countries, but certainly we were not exempt, and private means for promoting research, always our strongest point, had to be requisitioned. Under similar arrangements in Berlin, psychotherapy continued to advance.

Abroad as well as here the lay and medical public ask the question: How can psychanalysis ever hope to solve more than a small part of the psychoneurotic problem, with a system of individual treatment and prolonged analysis of the single case? This need not trouble us greatly if we but follow the wise course of the Berlin psychanalysts, who did not shrink from even small beginnings and were willing to devote the necessary time to the task. In 1919, operation of the Berlin Polyclinic began in a moderate way with three assistants and was privately financed over a term of years. Several volunteer assistants were added, but the burden of the work was carried by the full-time staff. Later, the staff increased to seven members who devoted jointly twenty-seven hours daily. This did not include the private analyses made by the Psychanalytic Union, a supporting outside group of psychanalysts, nor analyses made under the clinic's control by students. In three years the Polyclinic found itself pressed for space beyond the five rooms at its disposal.

As the number of patients increased, the Polyclinic required an almost continuous increase in the numbers of its staff, and the question arose in regard to training assistants. This was the second aim with which the staff entered on the foundation of the institute. It is a firm and well founded conviction that no person who has not been analyzed should become a practicing psychanalyst. Passive self analysis is therefore given in the latter part of the course, after intensive theoretic preparation. In 1920-1922, twenty-five pupils, including several physicians and teachers, were analyzed. Consultations with suitable patients were then entrusted to pupils, who were allowed to take the first steps of analysis alone and required to keep an accurate record; with this as a guide the teachers were readily able to make corrections. In

this way the host of errors made by the beginner, due to defective comprehension of the aims and methods of analysis and too rigid adherence to single findings, was avoided.

The patients comprise the intelligent and professional class as well as the lower middle class of working people, of all ages. Interviews covered three-quarters or one hour, and the patients came on an average three or four times a week; they were seen oftener in severe cases. One hundred and thirty-three analyses were carried out, and in 1922 Dr. Eitingen was able to make a formal statistical report. The question of hastening the treatment was given constant consideration, but has met with little success. The Polyclinic is satisfied with the results of its teaching activities, for the pupils have learned much and well, and have demonstrated the soundness of the idea.

Though the organizing of such clinics or institutes differs from that of other medical clinics, they are in this country not only feasible and practicable, but also a matter of the utmost urgency. I do not believe they should be organized on the lines of or be an integral part of the ordinary mental clinic at the outset; later, when their didactic functions come to the fore, the need of close affiliation with neuropsychiatry and psychiatry will be obvious.

In conclusion I submit: (1) that psychanalytic clinics are necessary for the therapeutic alleviation of the large mass of neurotic patients who cannot afford to pay for psychanalysis as now practiced; (2) that such clinics are necessary for maintaining a consistent school in the training of psychiatrists and psychanalysts, and thus obviating the present tendency to quackery in this specialty; (3) that these clinics should be independent in organization, but allied to our medical schools and hospitals; (4) that full time service of the resident staff should be expected, with a controlling or advisory board of analysts to support and give direction to the therapeutic and didactic work of the clinic.

DISCUSSION

Dr. Gilbert V. Hamilton (by invitation): The issue that Dr. Clark has defined here, viz., the need for psychanalytic clinics, is strikingly exemplified by the findings of the Division for Psychobiological Research of the Bureau of Social Hygiene. In it we deal largely with young married college graduates who are living on incomes of less than $5,000 a year. Many of them disclose maladjustments of one sort or another in the marital relationship, and are obviously in need of what the quite limited number of adequately trained New York psychanalysts have to give them. Unfortunately, they cannot pay half the fee per hour that I pay my dentist if they are to be given a sufficiently prolonged analysis to meet their needs. And yet they are young enough and plastic enough to be helped. Later, when their earnings may enable them to pay for psychanalysis, the damage will have been done. Some of them are drifting toward psychoneuroses and others toward the crystallization of attitudes which will make a satisfactory family life impossible.

Since the time for discussion is limited, I will touch only on one of the important points to be considered when we come to the establishment of psychanalytic clinics in New York. The problem of training psychanalysts in sufficient numbers to function in such clinics is very difficult. I am an objectivist, and not a psychanalyst, hence my view in the matter may be unduly prejudiced. I have come to regard psychanalysis as a subtle art and not a science, and to believe that only men of unusual capacity may safely practice it. Such men can take Freud's dogmatic assertions as guides to feeling their way into human situations which call for therapeutic endeavor, and thereby achieve

brilliant results in many cases. But they are so rare as to be practically negligible for the purposes that we should have in mind in establishing clinics in New York. If psychanalysts are to be trained in adequate numbers we must train them to function as technologists rather than as artists, which means that depth of insight must be sacrificed to soundness of tuitional procedure. The technologist must be taught to respect the rules of evidence that are observed in the natural sciences—a fact which has found profitable recognition in all other fields of medicine save in psychiatry. It may be contended, of course, that the psychanalyst would be unduly hampered in expressing his insights if he were required to respect scientific rules of evidence, but I believe an unprejudiced examination of the material of psychanalysis would disclose that from it could be elaborated a body of scientifically valid findings and safe rules for therapeutic procedure, which would go far toward solving the tuitional problem involved.

Mr. Earl F. Zinn (by invitation): The publicity that psychanalysis has received in this country is precipitating an important problem. Current fiction abounds in allusions, direct and indirect, to the marvels of this new thing. Semiscientific works on the subject have large sales. Among intelligent people, it is a popular topic of conversation. All this is not without import to psychanalysis and those who are seriously interested in its relations to science and medicine. It raises numerous problems, among which not the least important is that of meeting the demand with adequately trained analysts. The supply of analysts increases with the demand for analysis. Unfortunately, there is nothing in the operation of the law of supply and demand which touches the problem of the training and qualifications of the analysts. Dr. Clark's paper interests me, therefore, from this standpoint. Such a clinic or institute as he suggests would be a beginning in the development of a systematic program for training analysts under responsible supervision.

But more important even than the training of analysts is provision of facilities for research. Such an institute as is proposed can make its greatest and most lasting contribution if, as it is planned, a prominent place is given to the advancement of knowledge in this field. This means more than provision of facilities for investigation. It means that the spirit of research must be actively fostered.

Prof. E. C. Lindeman (by invitation): Using the proposed clinic for educational purposes would, it seems to me, be the most effective means of bringing psychanalysis into the stream of the medical sciences. I stand somewhere between Dr. Hamilton and the psychanalysts in attitude. I have maintained a critical attitude toward the whole development, but I am reminded that most sciences do start as arts, and the empirical pathway toward scientific verification is by no means the least important; it may be by means of this proposed clinic that scientific discoveries will be made tending to make psychanalysis verifiable by the general methods of accepted scientific method.

Mrs. Helen M. Ireland (by invitation): I am glad to contribute the impressions gathered from several years of work in a mental clinic in a small community. Primarily organized for the benefit of several agencies, the clinic has played a threefold part in serving its patients. The bulk of the work has naturally come from such groups as the Organized Charities, the Children's Bureau, the Red Cross and other allied agencies. The diagnoses have been made on the basis of medical, psychologic and social findings and the patients referred to social service with detailed recommendations for treatment. The adjusting of the individual's environment, the rearrangement of the points of

pressure and the mental therapy given during repeated clinic calls have often brought most encouraging results. Other demands on the clinic office have come from the professional and leisure classes who have brought their personal or family problems for discussion or advice. In these cases a mental hygiene society can do no more than act as a clearing house through which such persons are sent to psychiatrists or private sanatoriums. Between these two groups, however, is a smaller but most appealing set of young people who are so hampered with fears, depressions and hysterical difficulties that they are unable to make good. Here we find the undergraduate whose stuttering defeats all his social and academic aspirations, the teacher afraid to meet her classes, the eager volunteer whose neuritic right arm prevents the giving of acceptable service. It is this group, packed full with aspirations and possibilities, for which we have the greatest difficulty in securing suitable treatment. Social service in the free clinic offers no opportunity for relief, and the institutions that provide part or full foundation care have such long waiting lists they are unsuited for neuroses that need early treatment. It would seem indeed as if Dr. Clark's paper offers some solution for this difficult type of problem.

DR. C. P. OBERNDORF: At Homburg, Dr. Eitingen, director of the Berlin clinic, explained its workings in detail to Dr. Clark, Dr. Glueck and myself. I then went to Berlin to see the clinic in operation. It is entirely under the direction of the members of the Berlin Psychanalytic Society, is registered with the Board of Charities, and has permission from the state authorities to operate. As Dr. Clark said, when the war ended the need for such clinics was so acute that the state was quite ready to cooperate with any movement that would help the great number of neurotic patients then in Berlin. The clinic owes its success primarily to Dr. Eitingen, who has not only paid many of its expenses but also given his time unstintingly. There is no full time assistant, but each appointee devotes at least four hours a day to the work. Every member of the Berlin Psychanalytic Society has agreed to treat at least one clinic patient, either at the clinic or at his private office. The clinic has five rooms constantly in use. Each patient comes at least three times a week (some as many as four or five times) and is under analysis for an hour each time. The patients pay about $1.25 for the first visit, and thereafter the fee depends on the amount of money the patient can afford. Many are treated entirely free. To enable younger physicians to take the training, Dr. Eitingen personally pays them a small salary. All physicians must themselves have undergone psychanalysis before they are permitted to analyze others. A more recent corollary to this requirement is that a physician who has been analyzed must conduct the first analyses under the direction of a more experienced analyst so that the latter can forestall pitfalls into which the novice might stumble. The therapeutic successes of the clinic are good. Eighty or ninety analyses are conducted concurrently. Approximately 200 patients apply for treatment annually, of whom about half are accepted. Nearly one half of these complete their analyses. Thirty per cent. of the analyses completed are considered successful and about 70 per cent. of the patients analyzed are regarded as improved.

DR. A. A. BRILL: Dr. Clark's timely appeal is gratifying and, let us hope, will produce results. His paper gives the impression that the psychanalytic clinic is altogether new. Some of the members of the New York Psychanalytic Society have worked hard to bring into operation this very idea. As for its practical application, I feel that a psychanalytic clinic, independent of a medical school and without the active cooperation of the teachers, could not be a

success. For many years I have thought of this subject and investigated it thoroughly; I am convinced that such a clinic, especially for the training of physicians, must be connected with some institution for nervous and mental diseases. Unless one has good grounding in neurology and psychiatry, one is hardly fitted to be a psychanalytic therapist. Of this I am absolutely convinced. Analyses in a clinic do not differ in any way from analyses in private practice. The importance of the financial problem must be kept in mind. As Dr. Oberndorf has pointed out, the Berlin clinic is not only financed by Dr. Eitingen, but he, as well as a number of the leading analysts, give a great deal of their time to the clinics.

Dr. L. Pierce Clark: Owing to the rapidity with which I had to read my paper, I am afraid that Dr. Brill did not hear my opening remarks, in which I said I had nothing new or unique to present, but rather that the increasing urgency of establishing such clinics warrants its being stated and restated until there is some concerted and definite action taken by the medical profession as well as by laymen. As to the money needed, I have not the slightest doubt that money will be forthcoming as soon as we have organized ourselves for the work. The second point I am more doubtful about, and that is the approval by the average medical school of the coordinated activity of such a clinic in connection with its curriculum. That is the greatest difficulty at this time. If the schools had not rejected the question many years ago, there would not have been so many quacks practicing psychanalysis, and it would be under the control of well trained, careful practitioners.

Hysterical Depression. A Clinical and Psychanalytic Approach. Dr. Dorian Feigenbaum (by invitation).

Very colorful material was brought out during a psychanalysis lasting about seven months in a case of an atypical combination of conversion hysteria and depression. The patient, a girl, aged 24, a dressmaker, developed a neurosis immediately after her brother's death, at the age of 27, from cancer of the stomach. The patient nursed him during his sickness, which lasted eighteen months. She came for analysis one year after the outbreak of the neurosis. The patient was in a depressive state characterized by a self-centered mood, lack of interest in her surroundings, tense expression, sluggish gait and speech, inclination to cry, pessimistic ideas centering around the notion of death and a great variety of hypochondriacal fears and complaints. She feared that she was affected by every serious sickness known to her, ulcer of the stomach, ulcer of the brain, rheumatism, gallstones, anemia and cancer. Cancer was the most persistent fear. She complained of loss of appetite and pseudo-hunger, distaste of oil, butter, fat, etc.; "fulness" in throat, stomach and intestines; nausea and constipation; pressure, congestion in her breast, and difficulty in breathing. "I can't breathe," she complained, while resting quietly and speaking in a normal, even way. "It takes my breath away." For more than one year, as the history showed, she actually suffered from fluor albus. This stopped after six weeks of the analysis. Spells of spasms at night and occasional headaches complete the list. Most of her pains the patient localized in her left side. She was a victim of a number of compulsive fears ("of falling," "of fainting," "of being raped," "of drinking," "of bathing," "of cessation of menses," etc.); compulsive ideas ("pus in my mouth and throat," "I have dirt in my body," "I have bad imaginations," a kind of compulsive macropsy and "conglomeropsy"; she was compelled "to see several things conglomerated into one thing," "to see the colors perverted," i. e., "green for red," etc.); and com-

pulsive acts ("to examine and wash the mouth and throat several times a day for months," "to fill up my throat with water," "just to open my mouth," a compulsive bed-ceremony, etc.). All these symptoms may be gathered under the head of conversion hysteria, depression and a compulsive syndrome. Besides are to be noted visual hallucinations, observed exclusively in the first period of the analysis: "I saw a malicious woman," "a man in navy blue," "a girl in black, she cries," "small round green stones," "dead bodies," "pictures," "a man seducing a girl," "fire," etc.

The analysis was able to unfold the unconscious relations of almost all the symptoms, which are based on the patient's latent conflicts of the past as well as on the recent ones. Father-brother fixation and mother complex are in the center of her conflicts. A brother's death and a recent loss of a lover — because of the interference of a neighbor ("a malicious woman" or "that woman" in dreams and hallucinations) — provoked a latent neurosis of her childhood. As the fifth child in the family of six, from her earliest childhood she was under a continuous impression that in the family preference was given to the others, and thought that she was taken advantage of by her mother and her oldest brother. She definitely preferred her father and the younger of her brothers. She slept in one bed with father or older brother up to the age of about 12. One night, when she was 9 years old, her brother kept her tight in his arms; she awoke with anxiety and later refused to sleep with him again. "That night I saw the difference between men and girls," she reports. This traumatic experience contributing to her primary sex-envy forms the patient's castration-worry. Discontinuance of her libidinous father-investments of early childhood, active tendencies of castration (later resentments against mother and mother-images) and identification with men are the after-effects. The younger brother she identifies with the father. He brought her to America, married off her younger sister and was vitally interested in marrying her off when he took sick. During his sickness she nursed him and slept with him many nights "in order to be with him whenever he wanted her." (She always slept at his right side so that she felt him at her left side; the left side becomes to her a symbol of sickness and death). Shortly before his death the patient through an open door heard her brother saying to a friend: "I can't be saved any more; but she is to be saved." "I could not get what he meant," the patient reports, "What was I to be saved from? I did not feel sick at all. I was afraid he had become insane." (We trace here the "postponed obedience" which I believe in this case to be the leading factor in the neurosis and its fate.) Her first menstruation, at the age of 12, was a critical period. For several months she kept it a secret from her mother, probably because of the previous shock that she experienced in connection with blood and mother (a hemorrhage of the lips, which her mother laughed at, is a subject of continuous reproach toward mother "who neglected my whole life"), as well as because of an accident, a vaginal hemorrhage, which she had witnessed in a friend. Her resentment against her mother rose to its height when, at the age of 16, the mother interfered with her first love affair.

The patient has a very rich dream life. The psychanalytic work proceeded along the analysis of more than 150 dreams. Most of them centered around her brother-identification, her mother-complex and the castration-conflict. The brother appears as her beloved, with whom she desires to be in relation, regardless of the fact that he is dead. "Death" means to the dreamer's unconscious "death in love." Many of her dreams are typical exhibitionistic ones. Besides, the patient brings a great many cannibalistic dreams. The analysis of the

latter enabled an understanding of most of her oral and digestive symptoms and revealed the mechanism of introjection. The analysis proceeded most of the time by positive transference. The analyst was the missed brother. Periodically her negative disposition toward her mother was transferred. The patient's resistance was treated by virtue of her mother-dreams.

The following conclusions are made: The outbreak of the psychoneurosis follows the brother's death and the recent loss of her lover because they symbolize to her a new experience of castration. Have we a typical case of depression before us? No. Because there are absent the typical depressive inhibition and the typical impoverishment of the ego. We miss an exclusive regression of the libido to narcissistic positions. Is the patient's grief after her brother a melancholic grief? No. Freud's classic words, "In grief the world is poor and empty. In melancholia the ego is poor and empty," do not allow us to call this grief melancholic. The kaleidoscope of the conversion hysterical symptoms is also strange to a typical depression. On the other hand, we notice depressive elements, compulsive and hypochondriacal symptoms. The case is a typical combination of psychoneurosis with attributes of psychosis. The "postponed obedience" to a certain extent enables us to understand why this case did not become a psychosis. According to the dying brother's words, the patient had to become sick; she had to be saved. We see the brother's words serving as a command to her neurosis and at the same time giving her the ability to transfer which saved her from deeper regressions.

The patient now works in a shop and is sociable, though not yet amenable to mixing with new friends. She plans to go eventually to her mother and the rest of her family in Europe.

DISCUSSION

Dr. A. A. Brill: It is to be regretted that Dr. Feigenbaum could not give the whole analysis because of the lateness of the hour. Judging by the charts he has given, I can see that it is an interesting and well organized analysis. I wish, however, to put forward some objection to his term "hysterical melancholia." There is no such psychosis or neurosis, and I regret that this term should have been used. It seems to me that we are really dealing with a psychoneurosis having a pronounced schizoid background.

Dr. Feigenbaum: Dr. Brill was able to guess the structure of the psychoneurosis from the charts without knowing much of the case, as I was not able to represent it fully for lack of time. The first chart represents the patient's latent inner conflict from childhood until the outbreak of the neurosis. Due to specific shocks in connection with her mother, the primary Oedipus-conflict got a considerable power. Persons, regardless of sex, who treat her ill, as she believes, are her mother-images, and anger and resentment toward mother are transferred to them. You see such mother-images: the oldest brother and the younger sister (as from the etiologic series) and one brother-in-law, "that woman," her manager in the shop and later in the treatment the analyst (as from the symptomatic series). The objects of her first libidinous investments are: her father and her brother who brought her to America. Here again, early in childhood, the patient experienced serious shocks which caused an increase of the castration-complex and identification with men as father-brother-images. Withdrawal of libido from her first investments, as well as resentments toward her mother (active castration-tendencies), fall into suppression and form here a latent neurosis. The second chart represents the establishment of the psychoneurosis provoked by two incidents: the death of her brother and the loss of her lover. A new fatal deprivation of libido means to her

an irritation of the castration-worry which now urges her to find an outlet. She fails to find it in the reality, and the result is regression of the libido into infantile, partly narcissistic stages, that is, negation of the reality ("brother is not dead," "I did not lose my beloved") and reestablishment of previous investments. This is for the patient her "morbid gain." This morbid gain is overweighed by the symptoms as self-punishment, and follows the "postponed obedience."

To answer Dr. Brill's remark about the diagnosis, I call it a case of hysterical depression because there are present in the foreground conversion hysteria plus a hypochondriacal depression. Coming across the mechanism of introjection, Dr. Brill is justified in thinking of schizophrenia. This, of course, is of narcissistic nature. But I cannot diagnose the case as such a schizophrenia for the following reasons: The patient has no delusions, and her grief for her brother is not psychotic (we may call it a pseudomelancholic grief). Conversion hysteria appears in the center of the psychoneurosis and is not a concomitant. The hallucinations are of hysterical quality. For hysterical depression finally plead her insight into the disease and will of recovery, her good transference and the cure.

Book Reviews

ESSENTIALS OF PSYCHIATRY. By GEORGE W. HENRY, M.D. Price, $2.75. Pp. 199. Baltimore: Williams and Wilkins Company, 1925.

To write a textbook on psychiatry "for the general practitioner, for the student, for the nurse, for the social worker," and to crowd it into 200 pages, is an ambitious program, and something is bound to suffer. This is what has been attempted by Dr. Henry, and in addition, material has been included that might well be omitted, such as an alphabetical list of poisons that could conceivably (or inconceivably, e. g., brucine, snake-bite, verdigris) be obtained by patients. The section of clinical psychiatry is probably the least adequate, although there are good chapters on the development of personality and psychiatric treatment. The author relies on extracts from case records to prove his points, and on a hypothetic individual who, in order to emphasize the different types of personality disorders, runs the gauntlet of mental catastrophes. In the section on mental hygiene the author takes the reader by the hand and the two together advance along the devious pathway from infancy to adolescence and senility, with well meaning but presumably rather ineffectual parents in the background. "Our parents would realize that we are markedly curious, suggestible and imitative. They would know how deeply we are influenced by the general atmosphere of the home, and how readily we copy the general attitudes, manners and habits of older members of the family." Here we find directions for parents presented in an unusual and engaging form.

The classification of mental disorders is probably as good as any now in use. The author is up-to-date in including the minor mental maladies when dealing with the psychoses. Separate chapters are devoted to affective psychoses, schizophrenic psychoses, psychoneuroses, toxic psychoses, organic psychoses and constitutional inferiority. Throughout the book the importance of the sexual element in our lives is emphasized.

Treatment of psychotic and psychoneurotic patients is considered from many angles. A dozen different methods are briefly outlined and none is praised above its fellows. The impression is left that special training is important for all of them. Medical and surgical treatment are touched on, almost frowned on. Focal infection and the need for its elimination receive no specific mention. A chapter on psychiatric nursing by Adele Poston, R.N., is carefully written, but abounds in directions that could be carried out only by nurses trained in psychiatric hospitals. A short chapter on psychiatric history, while showing the notable advances in recent years, is perhaps too lurid for a work of this kind. The chapter on medicolegal aspects is too brief and general for the guidance of the average practitioner. The section on psychopathology of normal persons and the mental disorders of geniuses might well be omitted.

On the whole, the book presents the modern trend of psychiatry as it relates to general medicine. The explanation of mental mechanisms, while often involved, is such as to lift somewhat the veil of mystery and complexity that for the nonpsychiatrist shrouds the concept of insanity. Though the book is too severely compressed in some parts and unduly expanded in others, it makes interesting reading and gives to the general reader a commonsense view of psychiatry.

DIAGNOSTIK MIT FREIEM AUGE (EKTOSKOPIE). DR. EDUARD WEISZ. Second Edition. Price, 7:20 marks. Pp. 178. Berlin, Urban and Schwarzenberg, 1925.

In his preface Weisz explains what he means by the term "Ektoskopie," and he insists that there is a difference between "inspection" and "Ektoskopie."

Inspection, he says, is observation of the body changes in an ordinary way; but "Ektoskopie" is a particular technic in observation. For example, by the repeated enunciation of the word "Kitt" by the patient, movements of certain muscles become apparent in a particular and outstanding way, and therefore he thinks it is no longer ordinary inspection, but a more definite diagnostic procedure.

"Ektoskopie" is employed as an aid in diagnosis of pathologic changes in the organs of the thorax, abdomen and pelvis.

In neuropathology the author indicates its usefulness by employment of speech. Three factors cooperate in the production of speech: first, pressure by the abdomen which forces the air stream; second, laryngeal action, which regulates the amount of air that passes upward; third, the muscles of the palate, mouth and face, which modulate the air stream. All three factors produce a certain muscular rhythm. The first he calls the "Mimic" of the trunk, while the third, he designates as the "Mimic" of the face and neck.

These factors are seen only in the beginning of speech, disappearing suddenly with muscular rest, but this rest, Weisz concludes, is only apparent, since by the aid of motion pictures he found these visible muscles still in a state of tonic contraction unusual for striated muscle. He also states that in many affections of the abdominal organs the speech phenomena are absent on the abdomen over the place where the affected organ lies. He calls that a near reflex, and when the Mimic of the speech reflex in the abdominal muscles is missing, as in pleuritis, he calls it a far reflex.

It was this kind of observation that led Weisz to associate the speech phenomena with nervous disorders and neuropathology. He cites cases of hemiplegia in which the speech "Mimic" was absent on the paralyzed side of the trunk, and also in cases in which the patients apparently had recovered. This absence of the speech "Mimic" aided Weisz to locate central disease in an atypical hemiplegia, with obvious paralysis of the facial nerve only.

Weisz also records instances of hemiplegia in which the speech phenomenon on the paralyzed side was exaggerated and instances in persons with large and weak abdomens. He also found it absent in spastic conditions without paralysis. In such cases he had to resort to superficial palpation to establish the spasticity.

It is apparent from such discrepancies that the use of "Ektoskopie" by itself as a diagnostic means in neuropathology is as limited as ordinary eye observation.

AN INTRODUCTION TO THE MIND IN HEALTH AND DISEASE. FOR STUDENTS AND GENERAL PRACTITIONERS INTERESTED IN MENTAL WORK. By. T. WADDELOW SMITH, F.R.C.S. (England). Price, $4. New York City: William Wood & Company, 1925.

This book, while rather interesting, is a good example of the loose statements and careless reasoning characteristic of much of the recent literature of freudian or pseudo-freudian psychanalytic psychology. For example, in the preface, the author states that "many conclusions are drawn from what is purely hypothetical but in this work, for the sake of clearness, many of

these assumptions have been stated as if they were facts." To treat assumptions as proved facts may apparently increase clearness, but it makes the conclusions valueless. In the preface, the author describes mentation as "the functioning of the brain cells"; on page 71, he defines it as "primarily the functioning of the cells of the associative areas of the brain to nerve impulses from the extero-ceptors and intero-ceptors." This is only one of many examples of inaccuracy and carelessness.

He defines manic-depressive psychosis as "a psychosis characterized by instability of the emotional tone," which is no definition. Apparently the author produced this book because he was interested in the subject, but that he was entirely inadequate for the task must be as apparent to psychanalysts as to psychologists and psychiatrists of an older school.

THE ARCHIVES OF NEUROLOGY AND PSYCHIATRY is published by the American Medical Association to stimulate research in the field of diseases and disorders of the nervous system, and to disseminate knowledge in this department of medicine.

Manuscripts for publication, books for review, and correspondence relating to the editorial management should be sent to Dr. T. H. Weisenburg, Editor-in-Chief, 2037 Delancey St., Philadelphia, or to any other member of the Editorial Board. Communications regarding subscriptions, reprints, etc., should be addressed, ARCHIVES OF NEUROLOGY AND PSYCHIATRY, American Medical Association, 535 North Dearborn Street, Chicago.

Articles are accepted for publication on condition that they are contributed solely to the ARCHIVES OF NEUROLOGY AND PSYCHIATRY. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones of illustrations will be supplied by the Association when the original illustrations warrant.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index, published by the American Medical Association. This requires, in order given: name of author, title of article, name of periodical, with volume, page, month—day of month if weekly—and year. A complete list of abbreviations for standard periodicals, together with a full discussion of the style of the A. M. A. publications, appears in The Art and Practice of Medical Writing, a comprehensive book on the preparation of medical manuscripts, published by the American Medical Association. Price, $1.50.

Matter appearing in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY is covered by copyright, but, as a rule, no objection will be made to its reproduction in reputable medical journals if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY, or in any of the other publications issued by the Association, will not be permitted.

Authors will receive one hundred reprints free; additional reprints may be obtained at cost.

The ARCHIVES OF NEUROLOGY AND PSYCHIATRY is published monthly. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75, including postage. Single copies, 85 cents, postpaid.

Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

OTHER PERIODICAL PUBLICATIONS
of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Covers all the medical sciences and matters of general medical interest. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $6.50; foreign, $7.50. Single copies, 20 cents.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Devoted to the publication of advanced, original clinical and laboratory investigations in internal medicine. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $5.40; foreign, $5.75. Single copies, 75 cents.

AMERICAN JOURNAL OF DISEASES OF CHILDREN—Monthly. Presents pediatrics as a medical science and as a social problem. It includes carefully prepared collective abstracts based on recent pediatric literature, abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $4.00; Canadian, $4.30; foreign, $4.50. Single copies, 50 cents.

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY—Monthly. Devoted to advancing the knowledge of and progress in cutaneous diseases and syphilis. Publishes original contributions and full abstracts of the literature on these two subjects, transactions of the important dermatological societies, book reviews, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF SURGERY—Monthly. Devoted largely to the investigative and clinical phases of surgery, with monthly reviews on orthopedic and urologic surgery. Well illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF OTOLARYNGOLOGY—Monthly. A medium for the presentation of original articles on diseases of the ear, nose and throat, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

ARCHIVES OF PATHOLOGY AND LABORATORY MEDICINE—Monthly. A periodical devoted to the publication of original contributions in the field of pathology, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

QUARTERLY CUMULATIVE INDEX TO CURRENT MEDICAL LITERATURE—Quarterly. A complete subject and author index to the worthwhile current medical literature of the world. Issued four times a year. Fourth volume bound for permanent reference. Subscription price, calendar year: Domestic, $3.00; Canadian, $3.50; foreign, $3.75.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn St. CHICAGO

CONTENTS

PAGE

Neuron Destruction in Postencephalitic Paralysis Agitans: A Micrometric Study of the Lenticular Region and Substantia Nigra. J. Charnley McKinley, M.D., Minneapolis, and Lawrence R. Gowan, M.D., Duluth 1

Cerebral Symptoms Induced by Angioneurotic Edema. Foster Kennedy, M.D., F.R.S.E., New York 28

Trichinosis Encephalitis: A Pathologic Study. George B. Hassin, M.D., and Isadore B. Diamond, M.D., Chicago ... 34

Differential Diagnosis Between Cerebral Degeneration, Infiltrating Cerebral Neoplasm and Infiltrating Cerebral Neoplasm with Degeneration. Henry Alsop Riley, M.D., and Charles A. Elsberg, M.D., New York 48

Brain Repair. Richard B. Wilson, M.D., Boston 75

Hypophysial Fat Dystrophy with Hyperglycemia and Glycosuria: Report of a Case. Shepard Shapiro, M.D., and Mark G. Kliatshco, M.D., New York 85

Roentgen-ray Treatment of Pituitary Tumors. E. B. Towne, M.D., San Francisco 92

The Amyostatic Syndrome of Epidemic Encephalitis: Blood Sugar Tolerance Studies. Theophile Raphael, M.D., Olive M. Searle, M.S., and William G. Ferguson, M.D., Ann Arbor, Mich. 103

Clinical and Occasional Notes:

Thrombosis of the Rolandic Vein: Report of Case. Charles Edward Dowman, M.D., Atlanta, Ga. 110

News and Comments:

Congress of Alienists and Neurologists of France and of French Speaking Countries 113

Abstracts from Current Literature 114

Society Transactions:

New York Neurological Society 135

Book Reviews 148